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UTILITY PATENT APPLICATION TRANSMITTAL

(Only for new nonprovisional applications under 37 CFR 1,53(b))

Attorney Docket No.

2314-179

Total Pages

First Named Inventor or Application Identifier

Maren WATKINS Express Mail Label No.

APPLICATION ELEMENTS ADDRESS TO: Assistant Commissioner of Patents Box Patent Application See MPEP chapter 600 concerning utility patent application contents. Washington, D.C. 20231 6. [] Microfiche Computer Program (Appendix) Fee Transmittal Form (Submit an original, and a duplicate for fee processing) 2. [XX] Specification Total pages [851] 7. Nucleotide and/or Amino Acid Sequence Submission (preferred arrangement set forth below) (if applicable, all necessary) - Descriptive title of the invention a. [XX] Computer Readable Copy - Cross references to Related Applications - Statement Regarding Fed sponsored R&D b. [XX] Paper Copy (identical to computer copy) - Reference to Microfiche Appendix (139 pages) - Background of the Invention c. [XX] Statement verifying identity of above copies - Brief Summary of the Invention - Brief Description of the Drawings - Detailed Description ACCOMPANYING APPLICATION PARTS - Claims - Abstract of the Disclosure Assignment Papers (cover sheet & documents) Drawing(s) (35 USC 113) (Total Sheets) 3. I 1 37 CFR 3.73(b) Statement] Oath or Declaration (Total Pages) [] (when there is an assignee) a. [] Newly executed (original or copy) Power of Attorney b. [] Copy from a prior application 10 English Translation Document (if applicable) (37 CFR 1.63(d) 11 Ē Information Disclosure Statement /PTO 1449 (for continuation/divisional with Box 17 completed) Copies of IDS Citations [Note Box 5 below]] Preliminary Amendment i [] DELETION OF INVENTOR(S)

Signed statement attached deleting inventor(s) named in the prior application, see 37 CFR 1.63(d)(2) and 1.33(b) Incorporation by Reference (useable if Box 4b is checked) The entire disclosure of the prior application, from which a copy of the oath or declaration is supplied under Box 4b, is

considered as being part of the disclosure of the accompanying application and is hereby incorporated by reference therein.

13. [XX] Return Receipt Postcard (MPEP 503)

(Should be specifically itemized) 1 Small Entity Statement(s) 1 Statement Filed in prior application. Status still proper and desired Certified Copy of Priority Document(s).

(if foreign priority is claimed) 16. [1 Other:

17. If a CONTINUING APPLICATION, check appropriate box and supply the requisite information:

] Continuation [] Divisional [] Continuation-in-part (CIP) of prior application No.:

18. CORRESPONDENCE ADDRESS

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TITLE OF THE INVENTION ALPHA-CONOTOXIN PEPTIDES

CROSS-REFERENCE TO RELATED APPLICATION

The present application is related to U.S. provisional patent application Serial No. 60/118,381, filed 29 January 1999, incorporated herein by reference.

This invention was made with Government support under Grant No. PO1 GM48677 awarded by the National Institute of General Medical Sciences, National Institutes of Health, Bethesda, Maryland. The United States Government has certain rights in the invention.

BACKGROUND OF THE INVENTION

The invention relates to relatively short peptides (termed α -conotoxins herein), about 10-30 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include two disulfide bonds.

The publications and other materials used herein to illuminate the background of the invention, and in particular, cases to provide additional details respecting the practice, are incorporated by reference, and for convenience are referenced in the following text by author and date and are listed alphabetically by author in the appended bibliography.

The predatory cone snails (Conus) have developed a unique biological strategy. Their venom contains relatively small peptides that are targeted to various neuromuscular receptors and may be equivalent in their pharmacological diversity to the alkaloids of plants or secondary metabolites of microorganisms. Many of these peptides are among the smallest nucleic acidencoded translation products having defined conformations, and as such, they are somewhat unusual. Peptides in this size range normally equilibrate among many conformations. Proteins having a fixed conformation are generally much larger.

The cone snails that produce these peptides are a large genus of venomous gastropods comprising approximately 500 species. All cone snail species are predators that inject venom to capture prey, and the spectrum of animals that the genus as a whole can envenomate is broad. A wide variety of hunting strategies are used, however, every *Conus* species uses fundamentally the same basic pattern of envenomation.

Several peptides isolated from Conus venoms have been characterized. These include the α -, μ - and ω -conotoxins which target nicotinic acetylcholine receptors, muscle sodium channels,

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and neuronal calcium channels, respectively (Olivera et al., 1985). Conopressins, which are vasopressin analogs, have also been identified (Cruz et al.. 1987). In addition, peptides named conantokins have been isolated from Conus geographus and Conus tulipa (Mena et al., 1990; Haack et al., 1990).

The α-conotoxins are small peptides highly specific for neuromuscular junction nicotinic acetylcholine receptors (Gray et al., 1981; Marshall and Harvey, 1990; Blount et al., 1992; Jacobsen et al., 1997) or highly specific for neuronal nicotinic acetylcholine receptors (Fainzilber et al., 1994; Johnson et al., 1995; Cartier et al., 1996; Luo et al., 1998). The α-conotoxins with specificity for neuromuscular junction nicotinic acetylcholine receptors are used as neuromuscular blocking agents for use in conjunction with surgery, as disclosed in U.S. patent application Serial No. 09/ filed 21 January 2000 (Attorney Docket No. 2314-178.A) and international patent application No. PCT/US00/ , filed 21 January 2000 (Attorney Docket No. 2314-138.PCT), each incorporated by reference herein. Additional α-conotoxins and uses for them have been described in U.S. Patent Nos. 4,447,356 (Olivera et al., 1984); 5,432,155; 5,514,774, each incorporated herein by reference.

Additional uses for α-conotoxins are described in U.S. Serial No. 09/219,446, filed 22 December 1998, incorporated herein by reference. In this application, α-conotoxins with specificity for neuronal nicotinic acetylcholine receptors are used for treating disorders regulated at neuronal nicotinic acetylcholine receptors. Such disorders include, but are not limited to, cardiovascular disorders, gastric motility disorders, urinary incontinence, nicotine addiction, mood disorders (such as bipolar disorder, unipolar depression, dysthymia and seasonal effective disorder) and small cell lung carcinoma, as well as the localization of small cell lung carcinoma.

It is desired to provide additional α-conotoxin peptides having uses as described herein.

SUMMARY OF THE INVENTION

The invention relates to relatively short peptides (termed α-conotoxins herein), about 10-30 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include two disulfide bonds.

More specifically, the present invention is directed to a-conotoxin peptides having the general formula I:

Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Cys-Cys-Xaa6-Xaa7-Xaa8-Xaa9-Cys-Xaa10-Xaa11-Xaa12-Cys-Xaa₁ (SEO ID NO1:), wherein Xaa₁ is des-Xaa₁, Ile, Leu or Val; Xaa₂ is des-Xaa₂, Ala or Gly; Xaa₃ is des-Xaa, Gly, Trp (D or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid; Xaa, is des-

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Xaa4, Asp, Phe, Gly, Ala, Glu, γ-carboxy-Glu (Gla) or any unnatural aromatic amino acid; Xaa4 is Glu, Gla, Asp, Ala, Thr, Ser, Gly, Ile, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, Ophospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa, is Ser, Thr, Arg, ornithine, homoarginine, Lvs, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₂ is Asp, Glu, Gla, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₈ is Ser, Thr, Asn, Ala, Gly, His, halo-His, Pro or hydroxy-Pro; Xaa, is Thr, Ser, Ala, Asp, Asn, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₀ is Gly, Ser, Thr, Ala, Asn, Arg, ornithine, homoarginine, Lvs, N-methyl-Lvs, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₁ is Gln, Leu, His, halo-His, Trp (D or L), halo-Trp, neo-Trp, Tyr, nor-Tyr, mono-halo-Tyr, dihalo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid or any unnatural aromatic amino acid; Xaa₁₂ is Asn, His, halo-His, Ile, Leu, Val, Gln, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa12 is des-Xaa13, Val, He, Leu, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid. The C-terminus may contain a free carboxyl group or an amide group. The halo is chlorine, bromine or iodine, preferably iodine for Tyr and His and preferably bromine for Trp. The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L). The Tyr residues may be substituted with the 3-hydroxyl or 2-hydroxyl isomers and corresponding O-sulpho- and O-phosphoderivatives. The acidic amino acid residues may be substituted with any synthetic acidic bioisoteric amino acid surrogate, e.g., tetrazolyl derivatives of Gly and Ala.

More specifically, the present invention is directed to α -conotoxin peptides having the general formula II:

Xaa₁-Xaa₂-Xaa₃-Xaa₄-Cys-Cys-Xaa₅-Xaa₆-Xaa₁-Xaa₈-Cys-Xaa₉-Xaa₁₀-Xaa₁₁-Xaa₁₂-Xaa₁₃-Xaa₁₄-Cys-Xaa₁₅-Xaa₁₅-Xaa₁₇-Xaa₁₇-Xaa₁₇-Xaa₁₈-Xaa₁₈-Xaa₁₈-Xaa₁₈-Xaa₁₈-Xaa₁₉

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amino acid; Xaa6 is Asp, Asn, His, halo-His, Thr, Ser, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa7 is Pro or hydroxy-Pro; Xaa₈ is Ala, Ser, Thr, Asp, Val, Ile, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid: Xaao is Gly, Ile, Leu, Val, Ala, Thr, Ser, Pro, hydroxy-Pro, Phe, Trp (D or L), neo-Trp, halo-Trp, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid or any unnatural aromatic amino acid; Xaa10 is Ala, Asn, Phe, Pro, hydroxy-Pro, Glu, Gla, Gln, His, halo-His, Val, Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₁ is Thr. Ser. His, halo-His, Leu, Ile, Val, Asn, Met, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa₁₂ is Asn, Pro, hydroxy-Pro, Gln, Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa13 is des-Xaa13, Gly, Thr, Ser, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa14 is des-Xaa14, Ile, Val, Asp, Leu, Phe, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; and Xaa₁₅ is des-Xaa₁₅, Gly, Ala, Met, Ser, Thr, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N.N-dimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid; Xaa,6 is des-Xaa₁₆, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₇ is des-Xaa₁₇, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid. The C-terminus may contain a free carboxyl group or an amide group. The halo is preferably bromine, chlorine or iodine, more preferably iodine for His or Tyr and bromine for Trp. The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L). The Tyr residues may be substituted with the 3-hydroxyl or 2-hydroxyl isomers and corresponding O-sulpho- and O-

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phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic bioisoteric amino acid surrogate, e.g., tetrazolyl derivatives of Gly and Ala.

More specifically, the present invention is directed to α -conotoxin peptides having the general formula III:

Xaa1-Xaa2-Xaa3-Xaa4-Xaa5-Cys-Cys-Xaa6-Xaa7-Xaa8-Xaa9-Cys-Xaa10-Xaa11-Xaa12-Xaa13-Xaa₁₄-Xaa₁₅-Xaa₁₆-Cys-Xaa₁₇-Xaa₁₈-Xaa₂₀-Xaa₂₁-Xaa₂₂-Xaa₂₃-Xaa₂₄ (SEQ ID NO:3), wherein Xaa₁ is des-Xaa₁, Ser or Thr; Xaa₂ is des-Xaa₂, Asp, Glu, γ-carboxy-Glu (Gla), Asn, Ser or Thr; Xaa3 is des-Xaa3, Ala, Gly, Asn, Ser, Thr, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, Nmethyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa4 is des-Xaa, Ala, Val, Leu, Ile, Gly, Glu, Gla, Gln, Asp, Asn, Phe, Pro, hydroxy-Pro or any unnatural aromatic amino acid; Xaas is des-Xaas, Thr, Ser, Asp, Glu, Gla, Gln, Gly, Val, Asp, Asn, Ala, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N.N-dimethyl-Lys, N.N.Ntrimethyl-Lys or any unnatural basic amino acid; Xaa, is Thr, Ser, Asp, Asn, Met, Val, Ala, Gly, Leu, Ile, Phe, any unnatural aromatic amino acid, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa, is Ile, Leu, Val, Ser, Thr, Gln, Asn, Asp, Arg, His, halo-His, Phe, any unnatural aromatic amino acid, homoarginine, ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, Ophospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa₈ is Pro, hyroxy-Pro, Ser, Thr, Ile, Asp, Leu, Val, Gly, Ala, Phe, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N-trimethyl-Lys or any unnatural basic amino acid: Xaao is Val, Ala, Glv, Ile, Leu, Asp, Ser, Thr, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₀ is His, halo-His, Arg, homoarginine, ornithine, Lys, N-methyl-Lys, N,Ndimethyl-Lys, N.N.N-trimethyl-Lys, any unnatural basic amino acid, Asn, Ala, Ser, Thr, Phe, Ile, Leu, Gly, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid. Tyr, nor-Tyr, monohalo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa11 is Leu, Gln, Val, Ile, Gly, Met, Ala, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N.N.N-trimethyl-Lys, Ser, Thr. Arg, homoarginine, ornithine, any unnatural basic amino acid, Asn, Glu, Gla, Gln, Phe, Trp (D or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid; Xaa12 is Glu, Gla, Gln, Asn, Asp, Pro, hydroxy-Pro, Ser, Gly, Thr, Lys, N-methyl-Lys, N.N-dimethyl-Lys, N,N,N-trimethyl-Lys, Arg, homoarginine, ornithine, any unnatural basic amino acid, Phe, His, halo-

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His, any unnatural aromatic amino acid, Leu, Met, Gly, Ala, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa13 is His, halo-His, Asn, Thr, Ser, Ile, Val, Leu, Phe, any unnatural aromatic amino acid, Arg, homoarginine, ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Try, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa14 is Ser, Thr, Ala, Gln, Pro, hydroxy-Pro, Gly, Ile, Leu, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid; Xaa15 is Asn, Glu, Gla, Asp, Gly, His, halo-His, Ala, Leu, Gln, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,Ntrimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa16 is Met, Ile, Thr, Ser, Val, Leu, Pro, hydroxy-Pro, Phe, any unnatural aromatic amino acid, Tyr, nor-Tyr, monohalo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, any unnatural hydroxy containing amino acid, Glu, Gla, Ala, His, halo-His, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,Ndimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₇ is des-Xaa₁₇, Gly, Asp, Asn, Ala, Ile, Leu, Ser, Thr, His, halo-His, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,Ndimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid; Xaa18 is des-Xaa18, Gly, Glu, Gla, Gln, Trp (D or L), neo, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa19 is des-Xaa19, Ser, Thr, Val, Ile, Ala, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa20 is des-Xaa20, Val. Asp. His, halo-His, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa21 is des-Xaa21, Asn, Pro or hydroxy-Pro: Xaa22 is des-Xaa22, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa23 is des-Xaa23, Ser or Thr; Xaa24 is des-Xaa24, Leu, Ile or Val; with the proviso that (a) Xaa5 is not Gly, when Xaa1 is des-Xaa1, Xaa2 is des-Xaa₂, Xaa₃ is des-Xaa₃, Xaa₄ is des-Xaa₄, Xaa₆ is Ser, Xaa₇ is His, Xaa₈ is Pro, Xaa₉ is Ala, Xaa₁₀ is Ser, Xaa₁₁ is Val, Xaa₁₂ is Asn, Xaa₁₃ is Asn, Xaa₁₄ is Pro, Xaa₁₅ is Asp, Xaa₁₆ is Ile, Xaa₁₇ is des-Xaa₁₇, Xaa₁₈ is des-Xaa₁₈, Xaa₁₉ is des-Xaa₁₉, Xaa₂₀ is des-Xaa₂₀, Xaa₂₁ is des-Xaa₂₁, Xaa₂₂ is des-Xaa22, Xaa23 is des-Xaa23, and Xaa24 is des-Xaa24. The C-terminus may contain a free carboxyl group or an amide group. The halo is preferably bromine, chlorine or iodine, more preferably iodine for His and Tyr and bromine for Trp. The Cys residues may be in D or L configuration and may

optionally be substituted with homocysteine (D or L). The Tyr residues may be substituted with the 3-hydroxyl or 2-hydroxyl isomers and corresponding O-sulpho- and O-phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic bioisoteric amino acid surrogate, e.g., tetrazolyl derivatives of Gly and Ala.

The present invention is also directed to novel specific α -conotoxin peptides of general formula I having the formulas:

Asp-Xaa₁-Cys-Cys-Ser-Asp-Ser-Arg-Cys-Gly-Xaa₂-Asn-Cys-Leu (SEQ ID NO:4);
Ala-Cys-Cys-Ser-Asp-Arg-Arg-Cys-Arg-Xaa₃-Arg-Cys (SEQ ID NO:5);
Phe-Thr-Cys-Cys-Arg-Arg-Gly-Thr-Cys-Ser-Gln-His-Cys (SEQ ID NO:6);
Asp-Xaa₄-Cys-Cys-Arg-Arg-His-Ala-Cys-Thr-Leu-Ile-Cys (SEQ ID NO:7);

Asp-Xaa₄-Cys-Cys-Arg-Xaa₅-Xaa₅-Cys-Thr-Leu-lle-Cys (SEQ ID NO:8); Gly-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Arg-Xaa₄-Arg-Cys-Arg (SEQ ID NO:9);

Gly-Cly-Cys-Cys-Ser-Asp-Xaa₃-Arg-Cys-Ala-Xaa₃-Arg-Cys (SEQ ID NO:10);

IIe-Ala-Xaa₃-Asp-IIe-Cys-Cys-Ser-Xaa₁-Xaa₅-Asp-Cys-Asn-His-Xaa₂-Cys-Val (SEQ ID NO:11): and

Gly-Cys-Cys-Ser-Asp-Xaas-Arg-Cys-Xaas-His-Gln-Cys (SEQ ID NO:12), wherein Xaa1 is Glu or γ-carboxy-Glu (Gla); Xaa2 is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa3 is Trp (D or L), halo-Trp or neo-Trp; Xaa4 is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa, is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group. The halo is preferably bromine, chlorine or iodine, more preferably iodine for Tyr and bromine for Trp. In addition, the His residues may be substituted with halo-His; the Arg residues may be substituted by Lys, ornithine, homoargine, Nmethyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoargine, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; the Tyr residues may be substituted with any unnatural hydroxy containing amino acid; the Ser residues may be substituted with Thr; the Thr residues may be substituted with Ser; and the Phe and Trp residues may be substituted with any unnatural aromatic amino acid. The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L). The Tyr residues may be substituted with the 3-hydroxyl or 2-hydroxyl isomers and corresponding O-sulpho- and O-phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic bioisoteric amino acid surrogate, e.g., tetrazolyl derivatives of Gly and Ala.

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More specifically, the present invention is directed to the following α -conotoxin peptides of general formula I:

Im1.1: SEQ ID NO:4, wherein Xaa₁ is Glu and Xaa₂ is Lys;

Im1.2: SEQ ID NO:5, wherein Xaa₃ is Trp;

Rg1.2: SEQ ID NO:6;

Rg1.6: SEQ ID NO:7, wherein Xaa4 is Tyr;

Rg1.6A: SEQ ID NO:8, wherein Xaa4 is Tyr and Xaa5 is Pro;

Rg1.7: SEQ ID NO:9, wherein Xaa4 is Tyr and Xaa5 is Pro;

Rg1.9: SEQ ID NO:10, wherein Xaa3 is Trp and Xaa5 is Pro;

Rg1.10: SEQ ID NO:11, wherein Xaa₁ is Glu, Xaa₂ is Lys, Xaa₃ is Trp and Xaa₅ is

Pro; and

Rg1.11: SEQ ID NO:12, wherein Xaa2 is Lys and Xaa3 is Pro.

The C-terminus of Im1.1, Rg1.7 an Rg1.10 preferably contains a free carboxyl group. The C-terminus of Im1.2, Rg1.2, Rg1.6, Rg1.6A, Rg1.9 and Rg1.11 preferably contains an amide group.

The present invention is further directed to novel specific α -conotoxin peptides of general formula II having the formulas:

 $Cys\text{-}Cys\text{-}Ser\text{-}Asp\text{-}Xaa_5\text{-}Ala\text{-}Cys\text{-}Xaa_2\text{-}Gln\text{-}Thr\text{-}Xaa_5\text{-}Gly\text{-}Cys\text{-}Arg (SEQ ID NO:13);}$

 $Cys\text{-}Cys\text{-}Xaa_1\text{-}Asn\text{-}Xaa_5\text{-}Ala\text{-}Cys\text{-}Arg\text{-}His\text{-}Thr\text{-}Gln\text{-}Gly\text{-}Cys (SEQ ID NO:14)};$

 $Gly\text{-}Cys\text{-}Cys\text{-}Xaa_{3}\text{-}His\text{-}Xaa_{5}\text{-}Ala\text{-}Cys\text{-}Gly\text{-}Arg\text{-}His\text{-}Xaa_{4}\text{-}Cys\text{ (SEQ ID NO:15)};}$

Ala-Xaa₅-Cys-Cys-Asn-Asn-Xaa₅-Ala-Cys-Val-Xaa₂-His-Arg-Cys (SEQ ID NO:16);

 $Ala\text{-}Xaa_5\text{-}Gly\text{-}Cys\text{-}Cys\text{-}Asn\text{-}Asn\text{-}Xaa_5\text{-}Ala\text{-}Cys\text{-}Val\text{-}Xaa_2\text{-}His\text{-}Arg\text{-}Cys (SEQ ID NO:17)};$

 $Xaa_5\text{-}Xaa_5\text{-}Cys\text{-}Cys\text{-}Asn\text{-}Asn\text{-}Xaa_5\text{-}Ala\text{-}Cys\text{-}Val\text{-}Xaa_2\text{-}His\text{-}Arg\text{-}Cys (SEQ ID NO:18)};$

Asp-Xaa₁-Asn-Cys-Cys-Xaa₃-Asn-Xaa₅-Ser-Cys-Xaa₅-Arg-Xaa₅-Arg-Cys-Thr (SEQ ID

NO:19);

 $Gly\text{-}Cys\text{-}Cys\text{-}Ser\text{-}Thr\text{-}Xaa_5\text{-}Xaa_5\text{-}Cys\text{-}Ala\text{-}Val\text{-}Leu\text{-}Xaa_4\text{-}Cys (SEQ ID NO:20)};$

 $Gly\text{-}Cys\text{-}Cys\text{-}Gly\text{-}Asn\text{-}Xaa_5\text{-}Asp\text{-}Cys\text{-}Thr\text{-}Ser\text{-}His\text{-}Ser\text{-}Cys} \ (SEQ\ ID\ NO:21);$

Gly-Cys-Cys-Ser-Asn-Xaa₅-Xaa₅-Cys-Ala-His-Asn-Asn-Xaa₅-Asp-Cys-Arg (SEQ ID

NO:42);

 $Gly-Cys-Cys-Xaa_4-Asn-Xaa_5-Val-Cys-Xaa_2-Xaa_2-Xaa_4-Xaa_4-Cys-Xaa_3-Xaa_2 \quad (SEQ \quad ID \quad ID \quad (SEQ \quad (SEQ \quad ID \quad (SEQ \quad (SEQ \quad ID \quad (SEQ \quad (SEQ$

30 NO:154);

Xaa₃-Xaa₁-Xaa₃-Gly-Cys-Cys-Arg-His-Xaa₃-Ala-Cys-Gly-Xaa₂-Asn-Arg-Cys (SEQ ID NO:155);

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Cys-Cys-Ala-Asp-Xaa₃-Asp-Cys-Arg-Phe-Arg-Xaa₃-Gly-Cys (SEQ ID NO:156); Gly-Cys-Cys-Xaa₄-Asn-Xaa₅-Ser-Cys-Xaa₃-Xaa₂-Thr-Xaa₄-Cys-Ser-Xaa₃-Xaa₂ (SEQ ID NO:157);

Cys-Cys-Ser-Asn-Xaa₃-Thr-Cys-Xaa₂-Xaa₁-Thr-Xaa₄-Gly-Cys (SEQ ID NO:158);
Cys-Cys-Ala-Asn-Xaa₅-Ile-Cys-Xaa₂-Asn-Thr-Xaa₄-Gly-Cys (SEQ ID NO:159);
Cys-Cys-Asn-Asn-Xaa₅-Thr-Cys-Xaa₂-Xaa₁-Thr-Xaa₄-Gly-Cys (SEQ ID NO:160);
Cys-Cys-Ser-Asn-Xaa₅-Val-Cys-Xaa₂-Xaa₁-Thr-Xaa₄-Gly-Cys (SEQ ID NO:161);
Gly-Gly-Cys-Cys-Ser-Xaa₄-Xaa₅-Xaa₅-Cys-Ile-Ala-Ser-Asn-Xaa₅-Xaa₂-Cys-Gly (SEQ ID NO:162);

Gly-Cys-Cys-Ser-His-Xaa₃-Val-Cys-Ser-Ala-Met-Ser-Xaa₃-Ile-Cys (SEQ ID NO:163); Gly-Cys-Cys-Xaa₂-Asn-Xaa₃-Xaa₄-Cys-Gly-Ala-Ser-Xaa₂-Thr-Xaa₄-Cys (SEQ ID NO:164); Gly-Cys-Cys-Ser-Xaa₄-Xaa₃-Xaa₄-Cys-Phe-Ala-Thr-Asn-Xaa₅-Asp-Cys (SEQ ID NO:165); Gly-Gly-Cys-Cys-Ser-Xaa₄-Xaa₃-Xaa₃-Cys-Ile-Ala-Asn-Asn-Xaa₅-Leu-Cys-Ala (SEQ ID NO:166);

Gly-Gly-Cys-Cys-Ser-Xaa₄-Xaa₅-Cys-Ile-Ala-Asn-Asn-Xaa₅-Phe-Cys-Ala (SEQ ID NO:167);

Asp-Cys-Cys-Ser-Asn-Xaa₅-Xaa₅-Cys-Ser-Gln-Asn-Asn-Xaa₅-Asp-Cys-Met (SEQ ID NO:168); and

Asp-Cys-Cys-Ser-Asn-Xaa₅-Xaa₅-Cys-Ala-His-Asn-Asn-Xaa₅-Asp-Cys-Arg (SEQ ID NO:169).

wherein Xaa₁ is Glu or γ-carboxy-Glu (Gla); Xaa₂ is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa₃ is Trp (D or L), halo-Trp or neo-Trp; Xaa₄ is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa₅ is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group. The halo is preferably bromine, chlorine or iodine, more preferably iodine for Tyr and bromine for Trp. In addition, the His residues may be substituted with halo-His; the Arg residues may be substituted by Lys, ornithine, homoargine, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoargine, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; the Tyr residues may be substituted with any unnatural hydroxy containing amino acid; the Ser residues may be substituted with Thr; the Thr residues may be substituted with Ser; and the Phe and Trp residues may be substituted with any unnatural aromatic amino acid. The Cys residues may be in D or L configuration and may

optionally be substituted with homocysteine (D or L). The Tyr residues may be substituted with the 3-hydroxyl or 2-hydroxyl isomers and corresponding O-sulpho- and O-phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic bioisoteric amino acid surrogate, e.g., tetrazolyl derivatives of Gly and Ala.

More specifically, the present invention is directed to the following α -conotoxin peptides of general formula II:

of general formula II:	
Sn1.1:	SEQ ID NO:13, wherein Xaa2 is Lys and Xaa5 is Pro;
Sn1.2:	SEQ ID NO:14, wherein Xaa1 is Glu and Xaa5 is Pro;
SI1.3:	SEQ ID NO:15, wherein Xaa3 is Trp, Xaa4 is Tyr and Xaa5 is Pro;
A1.2:	SEQ ID NO:16, wherein Xaa2 is Lys and Xaa5 is Pro;
Bu1.1:	SEQ ID NO:17, wherein Xaa2 is Lys and Xaa5 is Pro;
Bu1.2:	SEQ ID NO:18, wherein Xaa2 is Lys and Xaa5 is Pro;
Bu1.3:	SEQ ID NO:19, wherein Xaa1 is Glu, Xaa3 is Trp and Xaa5 is Pro;
Bu1.4:	SEQ ID NO:20, wherein Xaa_4 is Tyr and Xaa_5 is Pro ;
Cr1.3:	SEQ ID NO:21, wherein Xaa ₅ is Pro;
Di1.1:	SEQ ID NO:42 wherein Xaa₃ is Pro;
Ms1.7:	SEQ ID NO:154, wherein Xaa_2 is Lys, Xaa_3 is Trp, Xaa_4 is Tyr and Xaa_5 is
	Pro;
P1.7:	SEQ ID NO:155, wherein Xaa_1 is Glu, Xaa_2 is Lys, Xaa_5 is Pro and Xaa_6 is
	Gln;
Ms1.2:	SEQ ID NO:156, wherein Xaa ₅ is Pro;
Ms1.3:	SEQ ID NO:157, wherein Xaa_2 is Lys, Xaa_3 is Trp, Xaa_4 is Tyr and Xaa_5 is
	Pro;
Ms1.4:	SEQ ID NO:158, wherein Xaa $_{\!\scriptscriptstyle 1}$ is Glu, Xaa $_{\!\scriptscriptstyle 2}$ is Lys, Xaa $_{\!\scriptscriptstyle 4}$ is Tyr and Xaa $_{\!\scriptscriptstyle 5}$ is
	Pro;
Ms1.5:	SEQ ID NO:159, wherein Xaa2 is Lys and Xaa3 is Pro;
Ms1.8:	SEQ ID NO:160, wherein Xaa $_{\!\scriptscriptstyle 1}$ is Glu, Xaa $_{\!\scriptscriptstyle 2}$ is Lys, Xaa $_{\!\scriptscriptstyle 4}$ is Tyr and Xaa $_{\!\scriptscriptstyle 5}$ is
	Pro;
Ms1.9:	SEQ ID NO:161, wherein Xaa_1 is Glu, Xaa_2 is Lys, Xaa_4 is Tyr and Xaa_5 is
	Pro;
Bt1.7:	SEQ ID NO:162, wherein Xaa2 is Lys, Xaa4 is Tyr and Xaa5 is Pro;
Lv1.5:	SEQ ID NO:163, wherein Xaa ₅ is Pro;

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Vr1 2:

preferably contains an amide group.

Ms1.10:	SEQ ID NO:164, wherein Xaa_2 is Lys, Xaa_4 is Tyr and Xaa_5 is Pro;
Om1.1:	SEQ ID NO:165, wherein Xaa4 is Tyr and Xaa5 is Pro;
R1.6:	SEQ ID NO:166, wherein Xaa4 is Tyr and Xaa5 is Pro;
R1.7:	SEQ ID NO:167, wherein Xaa4 is Tyr and Xaa5 is Pro;
Vr1.1:	SEQ ID NO:168, wherein Xaa, is Pro; and

SEO ID NO:169, wherein Xaa, is Pro. The C-terminus preferably contains a carboxyl group for the peptides Sn1.1, Sn1.2, Cr1.3, Di1.1, Ms1.2, Ms1.4, Ms1.5, Ms1.8, Ms1.9, Vr1.1 and Vr1.2. The C-terminus of the other peptides

The present invention is also directed to novel specific α-conotoxin peptides of general formula III having the formulas:

Gly-Cys-Cys-Ser-Asn-Xaa₅-Val-Cys-His-Leu-Xaa₁-His-Ser-Asn-Met-Cys(SEQIDNO:22); Gly-Cys-Cys-Ser-Asn-Xaa₅-Val-Cys-Arg-Gln-Asn-Asn-Ala-Xaa₁-Xaa₄-Cys-Arg (SEQ ID NO:23);

Xaas-Gln-Cys-Cys-Ser-His-Xaas-Ala-Cys-Asn-Val-Asp-His-Xaas-Xaa;-Ile-Cys-Arg (SEQ ID NO:24):

Xaa₅-Xaa₁-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Ile-Cys-Arg (SEQ ID NO:25);

 $Xaa_{s}\text{-}Gln\text{-}Cys\text{-}Cys\text{-}Ser\text{-}His\text{-}Xaa_{s}\text{-}Ala\text{-}Cys\text{-}Asn\text{-}Val\text{-}Asp\text{-}His\text{-}Xaa_{s}\text{-}Xaa_{1}\text{-}Ile\text{-}Cys\text{-}Asp\text{ }(SEQ)$ ID NO:26);

Xaa₅-Arg-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Ile-Cys-Arg (SEQ ID NO:27):

Xaas-Gln-Cys-Cys-Ser-His-Xaas-Ala-Cys-Asn-Val-Asp-His-Xaas-Gly-Ile-Cys-Arg (SEQ ID NO:28):

Xaa,-Gln-Cvs-Cvs-Ser-His-Xaa,-Ala-Cvs-Asn-Val-Asp-His-Xaa,-Xaa,-Thr-Cys-Arg (SEQ ID NO:29):

Xaa,-Gln-Cvs-Cvs-Ser-His-Xaa,-Ala-Cvs-Asn-Val-Asp-His-Xaa,-Xaa,-Val-Cvs-Arg (SEQ ID NO:30);

Xaa.-Gln-Cvs-Cvs-Ser-His-Xaa.-Ala-Cvs-Asn-Ile-Asp-His-Xaa.-Xaa.-Ile-Cys-Arg (SEQ ID NO:31);

Xaas-Gln-Cys-Cys-Ser-His-Xaas-Ala-Cys-Asn-Val-Asp-His-Xaas-Xaas-Ile-Cys-Arg-Arg-Arg-Arg-Arg (SEQ ID NO:32);

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Gly-Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ala-Val-Asn-His-Xaa₅-Xaa₁-Leu-Cys (SEQ ID NO:33);

Gly-Cys-Cys-Ser-His-Xaa₃-Ala-Cys-Ser-Val-Asn-His-Xaa₃-Xaa₁-Leu-Cys(SEQIDNO:34); Gly-Cys-Cys-Ser-His-Xaa₃-Ala-Cys-Asn-Val-Asp-His-Xaa₃-Xaa₁-Ile-Cys(SEQIDNO:35); Gly-Cys-Cys-Ser-His-Xaa₃-Ala-Cys-Ser-Gly-Xaa₂-Thr-Gln-Xaa₁-Xaa₄-Cys-Arg-Xaa₁-Ser

(SEQ ID NO:36); Xaa,-Cvs-Cvs-Ser-His-Xaa,-Ala-Cvs-Ser-Glv-Asn-Asn-Xaa,-Xaa,-Phe-Cvs-Arg-Gln (SEO

ID NO:37);

Gly-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Gly-Asn-Asn-Xaa₅-Xaa₁-Phe-Cys-Arg-Gln (SEQ ID NO:38);

 $Gly-Cys-Cys-Ser-His-Xaa_5-Xaa_5-Cys-Ala-Met-Asn-Asn-Xaa_5-Asp-Xaa_4-Cys \quad (SEQ\quad ID \\ NO:39);$

 $\label{eq:Gly-Cys-Ser-His-Xaa} Gly-Cys-Cys-Ser-His-Xaa_5-Xaa_5-Cys-Phe-Leu-Asn-Asn-Xaa_5-Asp-Xaa_4-Cys \quad (SEQ\quad ID\ NO:40);$

 $Gly-Cys-Cys-Ser-Asn-Xaa_5-Xaa_5-Cys-Ile-Ala-Xaa_2-Asn-Xaa_5-His-Met-Cys-Gly \ (SEQ\ ID\ NO:41);$

Gly-Cys-Cys-Ser-Asn-Xaa₂-Ala-Cys-Ala-Gly-Asn-Asn-Xaa₃-His-Val-Cys-Arg-Gln (SEQ ID NO:43);

Gly-Cys-Cys-Ser-Arg-Xaa₃-Ala-Cys-Ile-Ala-Asn-Asn-Xaa₃-Asp-Leu-Cys (SEQIDNO:44); Gly-Cys-Cys-Ser-Asn-Xaa₃-Val-Cys-His-Val-Xaa₁-His-Xaa₃-Xaa₁-Leu-Cys-Arg-Arg-Arg-Arg (SEQ ID NO:45);

Gly-Gly-Cys-Cys-Ser-Phe-Xaa₃-Ala-Cys-Arg-Xaa₂-Xaa₃-Arg-Xaa₃-Arg-Xaa₁-Met-Cys-Gly(SEQ ID NO:46);

Xaa₃-Xaa₁-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Asn-Ser-Ser-His-Xaa₅-Xaa₁-Leu-Cys-Gly(SEQ ID NO:47);

Xaa₃-Gln-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Asn-Val-Gly-His-Xaa₅-Xaa₁-Leu-Cys-Gly(SEQ ID NO:48);

 $Xaa_s\text{-Val-Cys-Cys-Ser-Asp-Xaa}_s\text{-Arg-Cys-Asn-Val-Gly-His-Xaa}_s\text{-Xaa}_1\text{-Ile-Cys-Gly (SEQ ID NO:49)};$

Gly-Cys-Cys-Ser-Arg-Xaa₃-Xaa₃-Cys-Ile-Ala-Asn-Asn-Xaa₃-Asp-Leu-Cys (SEQ ID NO:50);

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Xaa₅-Gin-Cys-Cys-Ser-His-Leu-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Ile-Cys-Arg (SEQ ID NO:51);

Gly-Cys-Cys-Ser-Xaa₄-Phe-Asp-Cys-Arg-Met-Met-Phe-Xaa₅-Xaa₁-Met-Cys-Gly-Xaa₃-Arg (SEQ ID NO:52);

Gly-Gly-Cys-Cys-Ser-Phe-Ala-Ala-Cys-Arg-Xaa₂-Xaa₄-Arg-Xaa₅-Xaa₁-Met-Cys-Gly(SEQ ID NO:53);

 $Gly\text{-}Gly\text{-}Cys\text{-}Cys\text{-}Phe\text{-}His\text{-}Xaa_{3}\text{-}Val\text{-}Cys\text{-}Xaa_{4}\text{-}Ile\text{-}Asn\text{-}Leu\text{-}Leu\text{-}Xaa_{1}\text{-}Met\text{-}Cys\text{-}Arg\text{-}Gln\text{-}Arg (SEQ ID NO:54);}$

Ser-Ala-Thr-Cys-Cys-Asn-Xaa₄-Xaa₅-Cys-Xaa₄-Xaa₁-Thr-Xaa₄-Xaa₄-Xaa₁-Ser-Cys-Leu (SEQ ID NO:55);

Ala-Cys-Cys-Ala-Xaa₄-Xaa₅-Xaa₅-Cys-Phe-Xaa₁-Ala-Xaa₄-Xaa₅-Xaa₁-Arg-Cys-Leu (SEQ ID NO:56);

 $\label{eq:Asn-Ala-Xaa_1-Cys-Cys-Xaa_4-Xa$

 $Xaa_1\text{-}Cys\text{-}Cys\text{-}Thr\text{-}Asn\text{-}Xaa_5\text{-}Val\text{-}Cys\text{-}His\text{-}Ala\text{-}Xaa_1\text{-}His\text{-}Gln\text{-}Xaa_1\text{-}Leu\text{-}Cys\text{-}Ala\text{-}Arg\text{-}Arg\text{-}Arg\text{-}SeQ\text{-}ID\text{-}NO:170)};$

Gly-Cys-Cys-Ser-Asn-Xaa₃-Val-Cys-His-Leu-Xaa₁-His-Ser-Asn-Leu-Cys (SEQ ID NO:171);

Xaa₁-Cys-Cys-Thr-Asn-Xaa₃-Val-Cys-His-Val-Xaa₁-His-Gln-Xaa₁-Leu-Cys-Ala-Arg-Arg-Arg (SEQ ID NO:172);

Xaa₆-Xaa₁-Cys-Cys-Ser-Xaa₄-Xaa₅-Ala-Cys-Asn-Leu-Asp-His-Xaa₅-Xaa₁-Leu-Cys (SEQ ID NO:173);

Xaa₃-Xaa₁-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Asn-Ser-Thr-His-Xaa₅-Xaa₁-Leu-Cys-Gly(SEQ ID NO:174);

Leu-Asn-Cys-Cys-Met-Ile-Xaa₃-Xaa₃-Cys-Xaa₂-Xaa₂-Xaa₄-Gly-Asp-Arg-Cys-Ser-Xaa₁-Val-Arg (SEQ ID NO:175);

Ala-Phe-Gly-Cys-Cys-Asp-Leu-Ile-Xaa₅-Cys-Leu-Xaa₁-Arg-Xaa₄-Gly-Asn-Arg-Cys-Asn-Xaa₁-Val-His (SEQ ID NO:176);

Leu-Gly-Cys-Cys-Asn-Val-Thr-Xaa₃-Cys-Xaa₃-Xaa₁-Xaa₂-Xaa₄-Gly-Asp-Xaa₂-Cys-Asn-Xaa₁-Val-Arg (SEO ID NO:177);

Asp-Xaa₁-Cys-Cys-Ser-Asn-Xaa₅-Ala-Cys-Arg-Val-Asn-Asn-Xaa₅-His-Val-Cys-Arg-Arg-Arg (SEQ ID NO:178);

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Leu-Asn-Cvs-Cvs-Ser-Ile-Xaa,-Glv-Cvs-Xaa,-Asn-Xaa,-Xaa,-Asp-Arg-Cvs-Ser-Xaa,-Val-Arg (SEO ID NO:179);

Gly-Gly-Cys-Cys-Ser-His-Xaas-Val-Cys-Xaad-Phe-Asn-Asn-Xaas-Gln-Met-Cys-Arg (SEQ ID NO:180);

Gly-Gly-Cys-Cys-Ser-His-Xaa,-Val-Cys-Asn-Leu-Asn-Asn-Xaa,-Gln-Met-Cys-Arg (SEQ ID NO:181);

Gly-Cys-Cys-Ser-His-Xaa₅-Xaa₅-Xaa₄-Ala-Asn-Asn-Gln-Ala-Xaa₄-Cys-Asn (SEQ ID NO:182):

Gly-Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Val-Thr-His-Xaa₅-Xaa₁-Leu-Cys (SEQ ID NO:183):

Gly-Gly-Cys-Cys-Ser-Xaa₄-Xaa₅-Ala-Cys-Ser-Val-Xaa₁-His-Gln-Asp-Leu-Cys-Asp (SEQ ID NO:184):

Val-Ser-Cys-Cys-Val-Val-Arg-Xaa₅-Cys-Xaa₅-Ile-Arg-Xaa₄-Gln-Xaa₁-Xaa₁-Cys-Leu-Xaa₁-Ala-Asp-Xaas-Arg-Thr-Leu (SEO ID NO:185);

Xaa6-Asn-Cys-Cys-Ser-Ile-Xaa6-Gly-Cys-Xaa3-Xaa1-Xaa6-Asp-Xaa6-Cys-Ser-Xaa₁-Val-Arg (SEQ ID NO:186);

Gly-Cys-Cys-Ser-Asn-Xaa₅-Val-Cys-His-Leu-Xaa₁-His-Xaa₅-Asn-Ala-Cys (SEQ ID NO:187);

Gly-Cys-Cys-Ser-Asn-Xaa₅-Ile-Cys-Xaa₄-Phe-Asn-Asn-Xaa₅-Arg-Ile-Cys-Arg (SEQ ID NO:188):

Xaa₁-Cys-Cys-Ser-Gln-Xaa₅-Xaa₅-Cys-Arg-Xaa₃-Xaa₂-His-Xaa₅-Xaa₁-Leu-Cys-Ser (SEQ ID NO:189);

Gly-Cys-Cys-Ser-His-Xaas-Ala-Cys-Ala-Gly-Asn-Asn-Gln-His-Ile-Cys (SEQ ID NO:190); Glv-Cvs-Cvs-Ala-Val-Xaa₅-Ser-Cvs-Arg-Leu-Arg-Asn-Xaa₅-Asp-Leu-Cvs-Glv-Gly (SEQ ID NO:191);

Glv-Cvs-Cvs-Ser-His-Xaa₅-Ala-Cvs-Asn-Val-Asn-Asn-Xaa₅-His-Ile-Cvs(SEQIDNO:192); Gly (SEQ ID NO:193);

Asp-Ala-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Ser-Gly-Xaa₅-His-Gln-Asp-Leu-Cys (SEQ ID NO:194):

Xaa₁-Asp-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Leu-Cys (SEQ ID NO:195):

Gly-Cys-Cys-Ser-His-Xaa,-Ala-Cys-Ala-Gly-Ser-Asn-Ala-His-Ile-Cys (SEO ID NO:196): Xaa₁-Asp-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Met-Cys (SEQ ID NO:197):

Gly-Cys-Cys-Ser-His-Xaa,-Ala-Cys-Ala-Gly-Asn-Asn-Xaa,-His-Ile-Cys(SEOIDNO:198); Gly-Cys-Cys-Gly-Asn-Xaa_s-Ser-Cys-Ser-Ile-His-Ile-Xaa_s-Xaa_d-Val-Cys-Asn (SEQ ID NO:199);

Thr-Asp-Ser-Xaa₁-Cys-Cys-Leu-Asp-Ser-Arg-Cys-Ala-Gly-Gln-His-Gln-Asp-Leu-Cys-Gly (SEQ ID NO:200);

Glv-Cvs-Cvs-Ser-Asn-Xaa,-Xaa,-Xaa,-Ala-Asn-Asn-Gln-Ala-Xaa,-Cvs-Asn (SEO ID NO:201):

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Val-Asn-Asn-Xaa₅-Asp-Ile-Cys(SEQIDNO:202); Gly-Xaa₂-Cys-Cys-Ile-Asn-Asp-Ala-Cys-Arg-Ser-Xaa₂-His-Xaa₄-Gln-Xaa₄-Cys-Ser (SEQ ID NO:203):

Gly-Cys-Cys-Xaa,-Asn-Ile-Ala-Cys-Arg-Ile-Asn-Asn-Xaa,-Arg-Xaa,-Cys-Arg (SEO ID NO:204);

Gly-Cys-Cys-Ser-His-Xaa₄-Val-Cys-Arg-Phe-Asn-Xaa₄-Xaa₅-Xaa₄-Cys-Gly (SEQ ID NO:205);

Asp-Xaa₁-Cys-Cys-Ala-Ser-Xaa₅-Xaa₅-Cys-Arg-Leu-Asn-Asn-Xaa₅-Xaa₄-Val-Cys-His (SEQ ID NO:206);

Gly-Cys-Cys-Ser-Asn-Xaa₅-Val-Cys-Xaa₃-Gln-Asn-Asn-Ala-Xaa₁-Xaa₄-Cys-Arg-Xaa₁-Ser (SEQ ID NO:207);

Glv-Cvs-Cvs-Ser-His-Xaa₄-Zvs-Ala-Gln-Asn-Asn-Gln-Asp-Xaa₄-Cvs (SEO ID NO:208);

Glv-Cvs-Cvs-Ser-His-Xaa,-Ala-Cvs-Ser-Glv-Asn-Asn-Arg-Xaa,-Xaa,-Cvs-Arg-Xaa,-Ser (SEQ ID NO:209);

Asp-Xaa_c-Cvs-Cvs-Ser-Xaa_c-Asp-Cvs-Gly-Ala-Asn-His-Xaa_c-Xaa_c-Ile-Cvs-Gly(SEQ ID NO:210);

Xaa₁-Cys-Cys-Ser-Gln-Xaa₅-Xaa₅-Cys-Arg-Xaa₃-Xaa₅-His-Xaa₅-Xaa₁-Leu-Cys-Ser (SEQ ID NO:211);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ala-Gly-Asn-Asn-Xaa₅-His-Ile-Cys(SEQIDNO:212); Gly-Cys-Cys-Ser-Asp-Xaa₅-Ser-Cys-Asn-Val-Asn-Asn-Xaa₅-Asp-Xaa₄-Cys (SEQ ID NO:213);

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Xaa,-Xaa,-Cys-Cys-Ser-Asp-Xaa,-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Met-Cys-Arg (SEQ ID NO:214);

Glv-Glv-Cvs-Cvs-Ser-Asn-Xaas-Ala-Cvs-Leu-Val-Asn-His-Leu-Xaa₁-Met-Cys (SEQ ID NO:215):

Arg-Asp-Xaa_s-Cys-Cys-Phe-Asp-Xaa_s-Ala-Cys-Asp-Val-Asp-Xaa_s-Gln-Ile-Cys (SEQ ID NO:216):

Cys-Cys-Ser-Asp-Xaas-Ser-Cys-Xaas-Arg-Leu-His-Ser-Leu-Ala-Cys-Thr-Gly-Ile-Val-Asn-Arg (SEQ ID NO:217);

Cvs-Cvs-Thr-Asn-Xaac-Ala-Cvs-Leu-Val-Asn-Asn-Ile-Arg-Phe-Cys-Gly(SEQIDNO:218); Asp-Xaa₁-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-His-Gly-Asn-Asn-Arg-Asp-His-Cys-Ala (SEQ ID NO:219);

Asp-Cys-Cys-Ser-His-Xaas-Leu-Cys-Arg-Leu-Phe-Val-Xaas-Gly-Leu-Cys-Ile (SEQ ID NO:220);

Gly-Cys-Cys-Ser-His-Xaa₅-Val-Cys-Xaa₂-Val-Arg-Xaa₄-Xaa₅-Asp-Leu-Cys-Arg (SEQ ID NO:221);

Gly-Cys-Cys-Ser-His-Xaas-Ala-Cys-Asn-Val-Asn-Asn-Xaas-His-Ile-Cys(SEQIDNO:222); Gly-Cys-Cys-Ser-His-Xaa₅-Val-Cys-Xaa₂-Val-Arg-Xaa₄-Ser-Asp-Met-Cys (SEQ ID NO:223):

Gly-Gly-Cys-Cys-Ser-His-Xaas-Ala-Cys-Xaas-Val-His-Phe-Xaas-His-Ser-Cys (SEQ ID NO:224);

Val-Cys-Cys-Ser-Asn-Xaas-Val-Cys-His-Val-Asp-His-Xaas-Xaa1-Leu-Cys-Arg-Arg-Arg-Arg-Arg (SEQ ID NO:225);

Gly-Cys-Cys-Ser-His-Xaa5-Val-Cys-Asn-Leu-Ser-Asn-Xaa5-Gln-Ile-Cys-Arg (SEQ ID NO:226):

Xaa6-Xaa1-Cys-Cys-Ser-His-Xaa5-Ala-Cys-Asn-Val-Asp-His-Xaa5-Xaa1-Ile-Cys-Arg (SEQ ID NO:227);

Gly-Cys-Cys-Ser-Asn-Xaas-Ala-Cys-Leu-Val-Asn-His-Ile-Arg-Phe-Cys-Gly (SEQ ID NO:228);

Asp-Cys-Cys-Asp-Asp-Xaa₅-Ala-Cys-Thr-Val-Asn-Asn-Xaa₅-Gly-Leu-Cys-Thr (SEQ ID NO:229); and

Gly-Cys-Cys-Ser-Asn-Xaa₅-Xaa₅-Cys-Ile-Ala-Xaa₂-Asn-Xaa₅-His-Met-Cys-Gly-Gly-Arg-Arg (SEO ID NO:230),

wherein Xaa, is Glu or γ-carboxy-Glu (Gla); Xaa2 is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N.N.N-trimethyl-Lys; Xaa₃ is Trp (D or L), halo-Trp or neo-Trp; Xaa₄ is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa, is Pro or hydroxy-Pro; Xaa, is Gln or pyro-Glu; and the C-terminus contains a carboxyl or amide group. The halo is preferably bromine, chlorine or iodine, more preferably iodine for Tyr and bromine for Trp. In addition, the His residues may be substituted with halo-His; the Arg residues may be substituted by Lys, ornithine, homoargine, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoargine, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; the Tyr residues may be substituted with any unnatural hydroxy containing amino acid; the Ser residues may be substituted with Thr; the Thr residues may be substituted with Ser; and the Phe and Trp residues may be substituted with any unnatural aromatic amino acid. The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L). The Tyr residues may be substituted with the 3-hydroxyl or 2-hydroxyl isomers and corresponding O-sulpho- and Ophospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic bioisoteric amino acid surrogate, e.g., tetrazolyl derivatives of Gly and Ala.

More specifically, the present invention is directed to the following α -conotoxin peptides of general formula III:

	SmI:	SEQ ID NO:22, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
20	OB-29:	SEQ ID NO:23, wherein Xaa_1 is Glu, Xaa_3 is Tyr and Xaa_5 is Pro;
	Tx1.1:	SEQ ID NO:24, wherein Xaa1 is Glu and Xaa5 is Pro;
	R1.1A:	SEQ ID NO:25, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	R1.1B:	SEQ ID NO:26, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	Om-9:	SEQ ID NO:27, wherein Xaa1 is Glu and Xaa5 is Pro;
25	Om-10:	SEQ ID NO:28, wherein Xaa₅ is Pro;
	Om-21:	SEQ ID NO:29, wherein Xaa1 is Glu and Xaa5 is Pro;
	Om-25:	SEQ ID NO:30, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	Om-27:	SEQ ID NO:31, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	Om-28:	SEQ ID NO:32, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
30	Bt1.2:	SEQ ID NO:33, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	Bt1.4:	SEQ ID NO:34, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	Da1.1:	SEQ ID NO:35, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;

SEQ ID NO:36, wherein Xaa, is Glu, Xaa2 is Lys and Xaa5 is Pro;

	OB-20:	SEQ ID NO.50, wherein Ada, is Oit, Adaz is Lys and Ada; is 110,
	TI:	SEQ ID NO:37, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	TIB:	SEQ ID NO:38, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	Pn1.1:	SEQ ID NO:39, wherein Xaa, is Pro;
5	Pn1.2:	SEQ ID NO:40, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	T1:	SEQ ID NO:41, wherein Xaa2 is Lys and Xaa5 is Pro;
	TIA:	SEQ ID NO:43, wherein Xaa, is Pro;
	Da1.2:	SEQ ID NO:44, wherein Xaa, is Pro;
	Cr1.2:	SEQ ID NO:45, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
10	SI1.2:	SEQ ID NO:46, wherein Xaa ₁ is Glu, Xaa ₂ is Lys and Xaa ₃ is Pro;
<u></u>	Tx1.3:	SEQ ID NO:47, wherein Xaa, is Glu and Xaa, is Pro;
	Da1.3:	SEQ ID NO:48, wherein Xaa, is Glu and Xaa, is Pro;
	Da1.4:	SEQ ID NO:49, wherein Xaa1 is Glu, Xaa5 is Pro and Xaa6 is Gln;
i.	Tx1.2:	SEQ ID NO:50, wherein Xaa₅ is Pro;
15	Om-35:	SEQ ID NO:51, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
[2]	Sl1.1:	SEQ ID NO:52, wherein Xaa $_1$ is Glu, Xaa $_3$ is Trp, Xaa $_4$ is Tyr and Xaa $_5$ is
		Pro;
	Sl1.6:	SEQ ID NO:53, wherein Xaa $_{\!1}$ is Glu, Xaa $_{\!2}$ is Lys, Xaa $_{\!4}$ is Tyr and Xaa $_{\!5}$ is
P. S.		Pro;
20	SI1.7:	SEQ ID NO:54, wherein Xaa1 is Glu Xaa4 is Tyr and Xaa5 is Pro;
	Bt1.1:	SEQ ID NO:55, wherein Xaa1 is Glu Xaa4 is Tyr and Xaa5 is Pro;
	Bt:1.3:	SEQ ID NO:56, wherein Xaa1 is Glu Xaa4 is Tyr and Xaa5 is Pro;
	Bt1.5:	SEQ ID NO:57, wherein Xaa ₁ is Glu Xaa ₄ is Tyr and Xaa ₅ is Pro;
	A1.4:	SEQ ID NO:170, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
25	A1.5:	SEQ ID NO:171, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	A1.6:	SEQ ID NO:172, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
	Af1.1:	SEQ ID NO:173, wherein Xaa ₁ is Glu Xaa ₄ is Tyr, Xaa ₅ is Pro and Xaa ₆ is
		Gln;
	Af1.2:	SEQ ID NO:174, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
30	Ar1.2:	SEQ ID NO:175, wherein Xaa ₁ is Glu, Xaa ₂ is Lys, Xaa ₃ is Trp, Xaa ₄ is Try
		and Xaa ₅ is Pro;
	Ar1.3:	SEQ ID NO:176, wherein Xaa ₁ is Glu, Xaa ₄ is Tyr and Xaa ₅ is Pro;

OB-20:

SEQ ID NO:203, wherein Xaa, is Lys, Xaa, is Tyr and Xaa, is Pro;

Ms1.1:

		Ms1.6:	SEQ ID NO:204, wherein Xaa4 is Tyr and Xaa5 is Pro;
		O1.1:	SEQ ID NO:205, wherein Xaa2 is Lys, Xaa4 is Tyr and Xaa5 is Pro;
		O1.2:	SEQ ID NO:206, wherein Xaa1 is Glu, Xaa4 is Tyr and Xaa5 is Pro;
		O1.4:	SEQ ID NO:207, wherein Xaa $_1$ is Glu, Xaa $_3$ is Trp, Xaa $_4$ is Tyr and Xaa $_5$ is
	5		Pro;
		O1.7:	SEQ ID NO:208, wherein Xaa4 is Tyr and Xaa5 is Pro;
		O1.8:	SEQ ID NO:209, wherein Xaa1 is Glu, Xaa4 is Tyr and Xaa5 is Pro;
		Om1.2:	SEQ ID NO:210, wherein Xaa ₁ is Glu, Xaa ₄ is Tyr and Xaa ₅ is Pro;
		Om1.3:	SEQ ID NO:211, wherein Xaa_1 is Glu , Xaa_2 is Lys , Xaa_3 is Trp and Xaa_3 is
	10		Pro;
100	12	Om1.4:	SEQ ID NO:212, wherein Xaa, is Pro;
4		Om1.5:	SEQ ID NO:213, wherein Xaa4 is Tyr and Xaa5 is Pro;
100	1	Om1.6:	SEQ ID NO:214, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
9	1	P1.4:	SEQ ID NO:215, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
10		P1.5:	SEQ ID NO:216, wherein Xaa, is Pro;
Sup on		P1.6:	SEQ ID NO:217, wherein Xaa3 is Trp and Xaa5 is Pro;
17		P1.8:	SEQ ID NO:218, wherein Xaa, is Pro;
All The	0	Rg1.1:	SEQ ID NO:219, wherein Xaa ₁ is Glu and Xaa ₅ is Pro;
Stad.	# A	Rg1.3:	SEQ ID NO:220, wherein Xaa ₅ is Pro;
	20	Rg1.4:	SEQ ID NO:221, wherein Xaa2 is Lys, Xaa4 is Tyr and Xaa5 is Pro;
		Rg1.5:	SEQ ID NO:222, wherein Xaa ₅ is Pro;
		Rg1.8:	SEQ ID NO:223, wherein Xaa2 is Lys, Xaa4 is Tyr and Xaa5 is Pro;
		Sm1.4:	SEQ ID NO:224, wherein Xaa2 is Lys and Xaa5 is Pro;
		Sm1.5:	SEQ ID NO:225, wherein Xaa1 is Glu and Xaa5 is Pro;
	25	S1.5:	SEQ ID NO:226, wherein Xaa ₅ is Pro;
		Tx1.5:	SEQ ID NO:227, wherein Xaa ₁ is Glu, Xaa ₅ is Pro and Xaa ₆ is Gln;
		T1.1:	SEQ ID NO:228, wherein Xaa, is Pro;
		Vr1.3:	SEQ ID NO:229, wherein Xaa, is Pro; and
		Tb:	SEQ ID NO:230, wherein Xaa2 is Lys and Xaa5 is Pro.
	30	The C-terminus pr	eferably contains a carboxyl group for the peptides OB-29, Tx1.1, R1.1A, R1.1B,

Tb: SEQ ID NO:230, wherein Xaa₂ is Lys and Xaa₃ is Pro.
The C-terminus preferably contains a carboxyl group for the peptides OB-29, Tx1.1, R1.1A, R1.1B, Om-9, Om-10, Om-21, Om-25, Om-27, Om-28, Cr1.2, Om-35, Bt1.1, Bt1.3, Bt1.5, A1.4, A1.6, Ar1.2, Ar1.3, Ar1.4, Ar1.5, Ar1.6, Ca1.3, Ca1.4, Ep1.2, Lv1.9, O1.2, Om1.3, Om1.6, P1.6, Rg1.1,

Rg1.3, Rg1.4, Sm1.5, Tx1.5 and Vr1.3. The C-terminus of the other peptides preferably contains an amide group.

The present invention is also directed to the novel specific α -contoxin peptides having the formulas:

 $\label{eq:cys-Cys-Thr-Ile-Xaa_3-Ser-Cys-Xaa_4-Xaa_1-Xaa_2-Xaa_2-Xaa_2-Ile-Xaa_3-Ala-Cys-Val-Phe (SEQ\ ID\ NO:231)\ and$

Gly-Cys-Gly-Asn-Xaa₅-Ala-Cys-Ser-Gly-Ser-Ser-Xaa₂-Asp-Ala-Xaa₅-Ser-Cys (SEQ ID NO:232).

wherein Xaa₁ is Glu or γ-carboxy-Glu (Gla); Xaa₂ is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa₄ is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa₅ is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group. The halo is preferably bromine, chlorine or iodine, more preferably iodine for Tyr. In addition, the His residues may be substituted with halo-His; the Arg residues may be substituted by Lys, ornithine, homoargine, N-methyl-Lys, N,N-dimethyl-Lys, N,N-trimethyl-Lys or any unnatural basic amino acid; the Lys residues may be substituted by Arg, ornithine, homoargine, N-methyl-Lys, N,N-dimethyl-Lys, N,N-trimethyl-Lys or any unnatural basic amino acid; the Tyr residues may be substituted with any unnatural hydroxy containing amino acid; the Ser residues may be substituted with Thr; the Thr residues may be substituted with Ser; and the Phe residues may be substituted with any unnatural aromatic amino acid. The Cys residues may be in D or L configuration and may optionally be substituted with homocysteine (D or L). The Tyr residues may be substituted with the 3-hydroxyl or 2-hydroxyl isomers and corresponding O-sulpho- and O-phospho-derivatives. The acidic amino acid residues may be substituted with any synthetic acidic bioisoteric amino acid surrogate, e.g., tetrazolyl derivatives of Gly and Ala.

More specifically, the present invention is directed to the following α -conotoxin peptides:

- G1.2: SEQ ID NO:231, wherein Xaa₁ is Glu, Xaa₂ is Lys, Xaa₄ is Tyr and Xaa₅ is Pro; and
- Rg1.12: SEQ ID NO:232, wherein Xaa2 is Lys and Xaa5 is Pro.

The C-terminus of G1.2 preferably contains a carboxyl group, and the C-terminus of Rg1.12 preferably contains an amide group.

Examples of unnatural aromatic amino acid include, but are not limited to, such as nitro-Phe, 4-substituted-Phe wherein the substituent is C₁-C₃ alkyl, carboxyl, hyrdroxymethyl, sulphomethyl, halo, phenyl, -CHO, -CN, -SO₃H and -NHAc. Examples of unnatural hydroxy containing amino

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acid, include, but are not limited to, such as 4-hydroxymethyl-Phe, 4-hydroxyphenyl-Gly, 2,6-dimethyl-Tyr and 5-amino-Tyr. Examples of unnatural basic amino acids include, but are not limited to, N-1-(2-pyrazolinyl)-Arg, 2-(4-piperinyl)-Gly, 2-(4-piperinyl)-Ala, 2-[3-(2S)pyrrolininyl)-Gly and 2-[3-(2S)pyrrolininyl)-Ala. These and other unnatural basic amino acids, unnatural hydroxy containing amino acids or unnatural aromatic amino acids are described in Building Block Index, Version 3.0 (1999 Catalog, pages 4-47 for hydroxy containing amino acids and aromatic amino acids and pages 66-87 for basic amino acids; see also http://www.amino-acids.com/, incorporated herein by reference, by and available from RSP Amino Acid Analogues, Inc., Worcester, MA.

Optionally, in the peptides of general formulas I, II and III and the specific peptides described above, the Asn residues may be modified to contain an N-glycan and the Ser and Thr residues may be modified to contain an O-glycan. In accordance with the present invention, a glycan shall mean any N-, S- or O-linked mono-, di-, tri-, poly- or oligosaccharide that can be attached to any hydroxy, amino or thiol group of natural or modified amino acids by synthetic or enzymatic methodologies known in the art. The monosaccharides making up the glycan can include D-allose, D-altrose, D-glucose, D-mannose, D-gulose, D-idose, D-galactose, D-talose, D-galactosamine, D-glucosamine, D-N-acetyl-glucosamine (GlcNAc), D-N-acetyl-galactosamine (GalNAc), D-fucose or D-arabinose. These saccharides may be structurally modified, e.g., with one or more O-sulfate, O-phosphate, O-acetyl or acidic groups, such as sialic acid, including combinations thereof. The gylcan may also include similar polyhydroxy groups, such as D-penicillamine 2,5 and halogenated derivatives thereof or polypropylene glycol derivatives. The glycosidic linkage is beta and 1-4 or 1-3, preferably 1-3. The linkage between the glycan and the amino acid may be alpha or beta, preferably alpha and is 1-.

Core O-glycans have been described by Van de Steen et al. (1998), incorporated herein by reference. Mucin type O-linked oligosaccharides are attached to Ser or Thr (or other hydroxylated residues of the present peptides) by a GalNAc residue. The monosaccharide building blocks and the linkage attached to this first GalNAc residue define the "core glycans," of which eight have been identified. The type of glycosidic linkage (orientation and connectivities) are defined for each core glycan. Suitable glycans and glycan analogs are described further in U.S. Serial No. 09/420,797, filed 19 October 1999 and in PCT Application No. PCT/US99/24380, filed 19 October 1999, both incorporated herein by reference. A preferred glycan is Gal(β1-3)GalNAc(α1-).

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Optionally, in the peptides of general formulas I and II and the specific peptides described above, pairs of Cys residues may be replaced pairwise with Ser/(Glu or Asp) or Lys/(Glu or Asp) combinations. Sequential coupling by known methods (Barnay et al., 2000; Hruby et al., 1994; Bitan et al., 1997) allows replacement of native Cys bridges with lactam bridges.

The present invention is further directed to propeptides and nucleic acid sequences encoding the propeptides or peptides as described in further detail herein.

DETAILED DESCRIPTION OF THE INVENTION

The invention relates to relatively short peptides (termed α -conotoxins herein), about 10-30 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include two disulfide bonds.

The present invention, in another aspect, relates to a pharmaceutical composition comprising an effective amount of an α -conotoxin peptide. Such a pharmaceutical composition has the capability of acting as antagonists for nicotinic acetylcholine receptors. In one aspect, the α -conotoxins with specificity for neuromuscular junction nicotinic acetylcholine receptors are used as neuromuscular blocking agents for use in conjunction with surgery, as disclosed in U.S. patent application Serial No. 09/______, filed 21 January 2000 (Attorney Docket No. 2314-178.A) and international patent application No. PCT/US00/_____, filed 21 January 2000 (Attorney Docket No. 2314-138.PCT), each incorporated by reference herein. In a second aspect, additional α -conotoxins and uses for them have been described in U.S. Patent Nos. 4,447,356 (Olivera et al., 1984); 5,432,155; 5,514,774, each incorporated herein by reference.

In a third aspect additional uses for α -conotoxins are described in U.S. Serial No. 09/219,446, filed 22 December 1998, incorporated herein by reference. In this application, α -conotoxins with specificity for neuronal nicotinic acetylcholine receptors are used for treating disorders regulated at neuronal nicotinic acetylcholine receptors. Such disorders include, but are not limited to, cardiovascular disorders, gastric motility disorders, urinary incontinence, nicotine addiction, mood disorders (such as bipolar disorder, unipolar depression, dysthymia and seasonal effective disorder) and small cell lung carcinoma, as well as the localization of small cell lung carcinoma.

The α -conotoxin peptides described herein are sufficiently small to be chemically synthesized. General chemical syntheses for preparing the foregoing α -conotoxin peptides are described hereinafter. Various ones of the α -conotoxin peptides can also be obtained by isolation

and purification from specific *Comus* species using the technique described in U.S. Patent No. 4,447,356 (Olivera et al., 1984), the disclosure of which is incorporated herein by reference.

Although the α -conotoxin peptides of the present invention can be obtained by purification from cone snails, because the amounts of α -conotoxin peptides obtainable from individual snails are very small, the desired substantially pure α -conotoxin peptides are best practically obtained in commercially valuable amounts by chemical synthesis using solid-phase strategy. For example, the yield from a single cone snail may be about 10 micrograms or less of α -conotoxin peptide. By "substantially pure" is meant that the peptide is present in the substantial absence of other biological molecules of the same type; it is preferably present in an amount of at least about 85% purity and preferably at least about 95% purity. Chemical synthesis of biologically active α -conotoxin peptides depends of course upon correct determination of the amino acid sequence.

The α -conotoxin peptides can also be produced by recombinant DNA techniques well known in the art. Such techniques are described by Sambrook et al. (1989). The peptides produced in this manner are isolated, reduced if necessary, and oxidized to form the correct disulfide bonds.

One method of forming disulfide bonds in the conantokin peptides of the present invention is the air oxidation of the linear peptides for prolonged periods under cold room temperatures or at room temperature. This procedure results in the creation of a substantial amount of the bioactive, disulfide-linked peptides. The oxidized peptides are fractionated using reverse-phase high performance liquid chromatography (HPLC) or the like, to separate peptides having different linked configurations. Thereafter, either by comparing these fractions with the elution of the native material or by using a simple assay, the particular fraction having the correct linkage for maximum biological potency is easily determined. However, because of the dilution resulting from the presence of other fractions of less biopotency, a somewhat higher dosage may be required.

The peptides are synthesized by a suitable method, such as by exclusively solid-phase techniques, by partial solid-phase techniques, by fragment condensation or by classical solution couplings.

In conventional solution phase peptide synthesis, the peptide chain can be prepared by a series of coupling reactions in which constituent amino acids are added to the growing peptide chain in the desired sequence. Use of various coupling reagents, e.g., dicyclohexylcarbodiimide or diisopropylcarbonyldimidazole, various active esters, e.g., esters of N-hydroxyphthalimide or N-hydroxy-succinimide, and the various cleavage reagents, to carry out reaction in solution, with subsequent isolation and purification of intermediates, is well known classical peptide methodology.

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Classical solution synthesis is described in detail in the treatise, "Methoden der Organischen Chemie (Houben-Weyl): Synthese von Peptiden," (1974). Techniques of exclusively solid-phase synthesis are set forth in the textbook, "Solid-Phase Peptide Synthesis," (Stewart and Young, 1969), and are exemplified by the disclosure of U.S. Patent 4,105,603 (Vale et al., 1978). The fragment condensation method of synthesis is exemplified in U.S. Patent 3,972,859 (1976). Other available syntheses are exemplified by U.S. Patents No. 3,842,067 (1974) and 3,862,925 (1975). The synthesis of peptides containing γ -carboxyglutamic acid residues is exemplified by Rivier et al. (1987), Nishiuchi et al. (1993) and Zhou et al. (1996).

Common to such chemical syntheses is the protection of the labile side chain groups of the various amino acid moieties with suitable protecting groups which will prevent a chemical reaction from occurring at that site until the group is ultimately removed. Usually also common is the protection of an α -amino group on an amino acid or a fragment while that entity reacts at the carboxyl group, followed by the selective removal of the α -amino protecting group to allow subsequent reaction to take place at that location. Accordingly, it is common that, as a step in such a synthesis, an intermediate compound is produced which includes each of the amino acid residues located in its desired sequence in the peptide chain with appropriate side-chain protecting groups linked to various ones of the residues having labile side chains.

As far as the selection of a side chain amino protecting group is concerned, generally one is chosen which is not removed during deprotection of the α -amino groups during the synthesis. However, for some amino acids, e.g., His, protection is not generally necessary. In selecting a particular side chain protecting group to be used in the synthesis of the peptides, the following general rules are followed: (a) the protecting group preferably retains its protecting properties and is not split off under coupling conditions, (b) the protecting group should be stable under the reaction conditions selected for removing the α -amino protecting group at each step of the synthesis, and (c) the side chain protecting group must be removable, upon the completion of the synthesis containing the desired amino acid sequence, under reaction conditions that will not undesirably alter the peptide chain.

It should be possible to prepare many, or even all, of these peptides using recombinant DNA technology. However, when peptides are not so prepared, they are preferably prepared using the Merrifield solid-phase synthesis, although other equivalent chemical syntheses known in the art can also be used as previously mentioned. Solid-phase synthesis is commenced from the C-terminus of the peptide by coupling a protected α -amino acid to a suitable resin. Such a starting material can

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be prepared by attaching an α-amino-protected amino acid by an ester linkage to a chloromethylated resin or a hydroxymethyl resin, or by an amide bond to a benzhydrylamine (BHA) resin or paramethylbenzhydrylamine (MBHA) resin. Preparation of the hydroxymethyl resin is described by Bodansky et al. (1966). Chloromethylated resins are commercially available from Bio Rad Laboratories (Richmond, CA) and from Lab. Systems, Inc. The preparation of such a resin is described by Stewart and Young (1969). BHA and MBHA resin supports are commercially available, and are generally used when the desired polypeptide being synthesized has an unsubstituted amide at the C-terminus. Thus, solid resin supports may be any of those known in the art, such as one having the formulae -O-CH₂-resin support, -NH BHA resin support, or -NH-MBHA resin support. When the unsubstituted amide is desired, use of a BHA or MBHA resin is preferred, because cleavage directly gives the amide. In case the N-methyl amide is desired, it can be generated from an N-methyl BHA resin. Should other substituted amides be desired, the teaching of U.S. Patent No. 4,569,967 (Kornreich et al., 1986) can be used, or should still other groups than the free acid be desired at the C-terminus, it may be preferable to synthesize the peptide using classical methods as set forth in the Houben-Weyl text (1974).

The C-terminal amino acid, protected by Boc or Fmoc and by a side-chain protecting group, if appropriate, can be first coupled to a chloromethylated resin according to the procedure set forth in K. Horiki et al. (1978), using KF in DMF at about 60°C for 24 hours with stirring, when a peptide having free acid at the C-terminus is to be synthesized. Following the coupling of the BOC-protected amino acid to the resin support, the α -amino protecting group is removed, as by using trifluoroacetic acid (TFA) in methylene chloride or TFA alone. The deprotection is carried out at a temperature between about 0°C and room temperature. Other standard cleaving reagents, such as HCl in dioxane, and conditions for removal of specific α -amino protecting groups may be used as described in Schroder & Lubke (1965).

After removal of the α -amino-protecting group, the remaining α -amino- and side chain-protected amino acids are coupled step-wise in the desired order to obtain the intermediate compound defined hereinbefore, or as an alternative to adding each amino acid separately in the synthesis, some of them may be coupled to one another prior to addition to the solid phase reactor. Selection of an appropriate coupling reagent is within the skill of the art. Particularly suitable as a coupling reagent is N,N'-dicyclohexylcarbodiimide (DCC, DIC, HBTU, HATU, TBTU in the presence of HoBt or HoAt).

The activating reagents used in the solid phase synthesis of the peptides are well known in the peptide art. Examples of suitable activating reagents are carbodiimides, such as N,N'-diisopropylcarbodiimide and N-ethyl-N'-(3-dimethylaminopropyl)carbodiimide. Other activating reagents and their use in peptide coupling are described by Schroder & Lubke (1965) and Kapoor (1970).

Each protected amino acid or amino acid sequence is introduced into the solid-phase reactor in about a twofold or more excess, and the coupling may be carried out in a medium of dimethylformamide (DMF):CH₂Cl₂ (1:1) or in DMF or CH₂Cl₂ alone. In cases where intermediate coupling occurs, the coupling procedure is repeated before removal of the α -amino protecting group prior to the coupling of the next amino acid. The success of the coupling reaction at each stage of the synthesis, if performed manually, is preferably monitored by the ninhydrin reaction, as described by Kaiser et al. (1970). Coupling reactions can be performed automatically, as on a Beckman 990 automatic synthesizer, using a program such as that reported in Rivier et al. (1978).

After the desired amino acid sequence has been completed, the intermediate peptide can be removed from the resin support by treatment with a reagent, such as liquid hydrogen fluoride or TFA (if using Fmoc chemistry), which not only cleaves the peptide from the resin but also cleaves all remaining side chain protecting groups and also the α -amino protecting group at the N-terminus if it was not previously removed to obtain the peptide in the form of the free acid. If Met is present in the sequence, the Boc protecting group is preferably first removed using trifluoroacetic acid (TFA)/ethanedithiol prior to cleaving the peptide from the resin with HF to eliminate potential Salkylation. When using hydrogen fluoride or TFA for cleaving, one or more scavengers such as anisole, cresol, dimethyl sulfide and methylethyl sulfide are included in the reaction vessel.

Cyclization of the linear peptide is preferably affected, as opposed to cyclizing the peptide while a part of the peptido-resin, to create bonds between Cys residues. To effect such a disulfide cyclizing linkage, fully protected peptide can be cleaved from a hydroxymethylated resin or a chloromethylated resin support by ammonolysis, as is well known in the art, to yield the fully protected amide intermediate, which is thereafter suitably cyclized and deprotected. Alternatively, deprotection, as well as cleavage of the peptide from the above resins or a benzhydrylamine (BHA) resin or a methylbenzhydrylamine (MBHA), can take place at 0°C with hydrofluoric acid (HF) or TFA, followed by oxidation as described above.

The peptides are also synthesized using an automatic synthesizer. Amino acids are sequentially coupled to an MBHA Rink resin (typically 100 mg of resin) beginning at the C-

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terminus using an Advanced Chemtech 357 Automatic Peptide Synthesizer. Couplings are carried out using 1,3-diisopropylcarbodimide in N-methylpyrrolidinone (NMP) or by 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) and diethylisopro- pylethylamine (DIEA). The FMOC protecting group is removed by treatment with a 20% solution of piperidine in dimethylformamide(DMF). Resins are subsequently washed with DMF (twice), followed by methanol and NMP.

Pharmaceutical compositions containing a compound of the present invention or its pharmaceutically acceptable salts as the active ingredient can be prepared according to conventional pharmaceutical compounding techniques. See, for example, *Remington's Pharmaceutical Sciences*, 18th Ed. (1990, Mack Publishing Co., Easton, PA). Typically, an antagonistic amount of the active ingredient will be admixed with a pharmaceutically acceptable carrier. The carrier may take a wide variety of forms depending on the form of preparation desired for administration, e.g., intravenous, oral or parenteral. The compositions may further contain antioxidizing agents, stabilizing agents, preservatives and the like.

For oral administration, the compounds can be formulated into solid or liquid preparations such as capsules, pills, tablets, lozenges, melts, powders, suspensions or emulsions. In preparing the compositions in oral dosage form, any of the usual pharmaceutical media may be employed, such as, for example, water, glycols, oils, alcohols, flavoring agents, preservatives, coloring agents, suspending agents, and the like in the case of oral liquid preparations (such as, for example, suspensions, elixirs and solutions); or carriers such as starches, sugars, diluents, granulating agents, lubricants, binders, disintegrating agents and the like in the case of oral solid preparations (such as, for example, powders, capsules and tablets). Because of their ease in administration, tablets and capsules represent the most advantageous oral dosage unit form, in which case solid pharmaceutical carriers are obviously employed. If desired, tablets may be sugar-coated or enteric-coated by standard techniques. The active agent can be encapsulated to make it stable to passage through the gastrointestinal tract while at the same time allowing for passage across the blood brain barrier. See for example, WO 96/11698.

For parenteral administration, the compound may be dissolved in a pharmaceutical carrier and administered as either a solution or a suspension. Illustrative of suitable carriers are water, saline, dextrose solutions, fructose solutions, ethanol, or oils of animal, vegetative or synthetic origin. The carrier may also contain other ingredients, for example, preservatives, suspending

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agents, solubilizing agents, buffers and the like. When the compounds are being administered intrathecally, they may also be dissolved in cerebrospinal fluid.

The active agent is preferably administered in an therapeutically effective amount. The actual amount administered, and the rate and time-course of administration, will depend on the nature and severity of the condition being treated. Prescription of treatment, e.g. decisions on dosage, timing, etc., is within the responsibility of general practitioners or spealists, and typically takes account of the disorder to be treated, the condition of the individual patient, the site of delivery, the method of administration and other factors known to practitioners. Examples of techniques and protocols can be found in *Remington's Parmaceutical Sciences*. Typically the conopeptides of the present invention exhibit their effect at a dosage range from about 0.001 mg/kg to about 250 mg/kg, preferably from about 0.05 mg/kg to about 100 mg/kg of the active ingredient, more preferably from a bout 0.1 mg/kg to about 75 mg/kg. A suitable dose can be administered in multiple sub-doses per day. Typically, a dose or sub-dose may contain from about 0.1 mg to about 500 mg of the active ingredient per unit dosage form. A more preferred dosage will contain from about 0.5 mg to about 100 mg of active ingredient per unit dosage form. Dosages are generally initiated at lower levels and increased until desired effects are achieved.

Alternatively, targeting therapies may be used to deliver the active agent more specifically to certain types of cell, by the use of targeting systems such as antibodies or cell specific ligands. Targeting may be desirable for a variety of reasons, e.g. if the agent is unacceptably toxic, or if it would otherwise require too high a dosage, or if it would not otherwise be able to enter the target cells.

The active agents, which are peptides, can also be administered in a cell based delivery system in which a DNA sequence encoding an active agent is introduced into cells designed for implantation in the body of the patient, especially in the spinal cord region. Suitable delivery systems are described in U.S. Patent No. 5,550,050 and published PCT Application Nos. WO 92/19195, WO 94/25503, WO 95/01203, WO 95/05452, WO 96/02286, WO 96/02646, WO 96/40871, WO 96/40959 and WO 97/12635. Suitable DNA sequences can be prepared synthetically for each active agent on the basis of the developed sequences and the known genetic code.

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EXAMPLES

The present invention is described by reference to the following Examples, which are offered by way of illustration and are not intended to limit the invention in any manner. Standard techniques well known in the art or the techniques specifically described below were utilized.

EXAMPLE 1

Isolation of α-Conotoxins

Crude venom was extracted from venom ducts (Cruz et al., 1976), and the components were purified as previously described (Cartier et al., 1996a). The crude extract from venom ducts was purified by reverse phase liquid chromatography (RPLC) using a Vydac C_{18} semi-preparative column (10 x 250 mm) and elution with a linear gradient of acetonitrile in 0.1% TFA. Further purification of bioactive peaks was done on a Vydac C_{18} analytical column (4.6 x 220 mm) eluted with a gradient of acetonitrile in 0.1% TFA. The effluents were monitored at 220 nm. Peaks were collected, and aliquots were assayed for activity. Activity was monitored by assessing block of $\alpha 3\beta 4$ nAChRs expressed in *Xenopus* oocytes.

The amino acid sequence of the purified peptides were determined by standard methods. The purified peptides were reduced and alkylated prior to sequencing by automated Edman degradation on an Applied Biosystems 477A Protein Sequencer with a 120A Analyzer (DNA/Peptide Facility, University of Utah) (Martinez et al., 1995; Shon et al., 1994).

In accordance with this method, peptides MII, AuIA, AuIB, AuIC, MAR-1, MAR-2, TI, OB-29, EpI, S1.1, Bn1.1, Bn1.2, Ca1.1, Ca1.2, Cn1.1, Cn1.2 and Sm1.3 were obtained.

EXAMPLE 2

Synthesis of Conopeptides

The synthesis of conopeptides, either the mature toxins or the precursor peptides, was separately performed using conventional protection chemistry as described by Cartier et al. (1996). Briefly, the linear chains were built on Rink amide resin by Fmoc procedures with 2-(1H-benzotriol1-yl)-1,1,3,3,-tetramethyluronium tetrafluoroborated coupling using an ABI model 430A peptide sythesizer with amino acid derivatives purchased from Bachem (Torrence CA). Orthogonal protection was used on cysteines: Cys³ and Cys ¹⁶ were protected as the stable Cys(S-acetamidomethyl), while Cys² and Cys⁸ were protected as the acid-labile Cys(S-trityl). After removal of the terminal Fmoc protecting group and cleavage of the peptides from the resins, the

released peptides were precipitated by filtering the reaction mixture into -10°C methyl t-butyl ether. which removed the protecting groups except on Cys3 and Cys16. The peptides were dissolved in 0.1% TFA and 60% acetonitrile and purified by RPLC on a Vydac C₁₈ preparative column (22 x 250 mm) and eluted at a flow rate of 20 mL/min with a gradient of acetonitrile in 0.1% TFA.

The disulfide bridges in the three conopeptides were formed as described in Cartier et al. (1996). Briefly, the disulfide bridges between Cys2 and Cys8 were formed by air oxidation which was judged to be complete by analytical RPLC. The monocyclic peptides were purified by RPLC on a Vydac C₁₈ prepartive column (22 x 250 mm) and eluted with a gradient of acetonitrile in 0.1% TFA. Removal of S-acetamidomethyl groups and closure of the disulfide bridge between Cys3 and Cys16 was carried out simultaneously be iodine oxidation. The cyclic peptides were purified by RPLC on a Vydac C₁₈ prepartive column (22 x 250 mm) and eluted with a gradient of acetonitrile in 0.1% TFA.

EXAMPLE 3

Isolation of DNA Encoding α-Conotoxins

DNA coding for α-conotoxins was isolated and cloned in accordance with conventional techniques using general procedures well known in the art, such as described in Olivera et al. (1996). Alternatively, cDNA libraries was prepared from Conus venom duct using conventional techniques. DNA from single clones was amplified by conventional techniques using primers which correspond approximately to the M13 universal priming site and the M13 reverse universal priming site. Clones having a size of approximately 300 nucleotides were sequenced and screened for similarity in sequence to known α-conotoxins. The DNA sequences and encoded propeptide or peptide sequences are set forth in Tables 1-134.

TABLE 1

	DN	A Se	quen	ce (S	EQ II	DNC):58)	and	Prote	ın Se	quen	ce (S	EQ II	DNC):59)	of MII
25			acc Thr													
			tca Ser													
30			tct Ser													
			tgt Cys													

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TABLE 2

DNA Sequence (SEQ ID NO:60) and Protein Sequence (SEQ ID NO:61) of AuIA atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca gat cgt gca tct gat ggc agg aag gac gca gcg tct ggc Phe Thr Ser Asp Arg Ala Ser Asp Gly Arg Lys Asp Ala Ala Ser Gly ctg acc gct ctg acc atc aag gga tgc tgt tct tat cct ccc tgt tc Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser Tyr Pro Pro Cys Phe gcg act aat tca gac tat tgt ggt tgacgacgct gatgctccag gaccctctga Ala Thr Asn Ser Asp Tyr Cys Gly

TABLE 3

DNA Sequence (SEQ ID NO:62) and Protein Sequence (SEQ ID NO:63) of AuIB atg tto acc gtg ttt ctg ttg gtc gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca gat cgt gca tct gag agc agc acg acg cg gcc phe Thr Ser Asp Arg Ala Ser Asp Gly Arg Lys Asp Ala Ala Ser Gly ctg att gct ctg acc atg aag gag gcg cct gtt ctc att cct ccc tgt ttc Leu Tie Ala Leu Thr Met Lys Gly Cys Cys Ser Tyr Pro Pro Cys Phe gcg act aat cca gac tgt ggt cga cga cgc tgatgctcca ggaccctctg Ala Thr Asn Pro Asp Cys Gly Arg Arg Arg aaccacgacg t

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TABLE 4

DNA Sequence (SEQ ID NO:64) and Protein Sequence (SEQ ID NO:65) of Tx1.3 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser tct tct tca ggt cgt agt aca ttt cgt ggc agg aat gcc gca gcc aaa Phe Ser Ser Gly Arg Ser Thr Phe Arg Gly Arg Asa Ala Ala Ala Lys gcg tct ggc ctg gtc agt ctg act gac aga aga cca gaa tgc tgt agt Ala Ser Gly Leu Val Ser Leu Thr Asp Arg Arg Pro Glu Cys Cys Ser gat cct cgc tgt aac tcg agt cat cca gaa ctt tgt ggt gga aga cgc Asp Pro Arg Cys Asn Ser Ser His Pro Glu Leu Cys Gly Gly Arg Arg tgatgctcca ggaccctctg aaccacagacg t

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TABLES

	TABLE 5
	DNA Sequence (SEQ ID NO:66) and Protein Sequence (SEQ ID NO:67) of Tx1.2
	atg tto acc gtg ttt ctg ttg gtt gtc ttg gca acc gcc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Ala Val Val Ser
5	ttc act tca gat cgt gca tct gat gac ggg aaa gcc gct gcg tct gac Phe Thr Ser Asp Arg Ala Ser Asp Asp Gly Lys Ala Ala Ala Ser Asp
	ctg atc act ctg acc atc aag gga tgc tgt tct cgt cct ccc tgt atc Leu Ile Thr Leu Thr Ile Lys Gly Cys Cys Ser Arg Pro Pro Cys Ile
10	gcg aat aat cca gac ttg tgt ggt tgacgacgct gatgctccag aacggtctga Ala Asn Asn Pro Asp Leu Cys Gly
	accacgacgt togagcaatg ttcaccgtgt ttctgttggt tgtctt
(2	TABLE 6
+3 -#	DNA Sequence (SEQ ID NO:68) and Protein Sequence (SEQ ID NO:69) of Tx1.1
15 115	atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser
ei ei	tto act toa ggt ogt agt aca ttt ogt ggo agg aat goo goa goo aaa Phe Thr Ser Gly Arg Ser Thr Phe Arg Gly Arg Asn Ala Ala Ala Lys

N 20 N C

TABLE 6

DNA Sequence (SEQ ID NO:68) and Protein Sequence (SEQ ID NO:69) of Tx1.1 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca ggt cgt agt aca ttt cgt ggc agg aat gcc gca gcc aaa Phe Thr Ser Gly Arg Ser Thr Phe Arg Gly Arg Asn Ala Ala Ala Lys gcg tot ggc ctg gtc agt ctg act gac agg aga cca caa tgc tgt tot Ala Ser Gly Leu Val Ser Leu Thr Asp Arg Arg Pro Gln Cys Cys Ser cat cct ccc tgt aac gta gat cat cca gaa att tgt cgt tgaagacgct His Pro Ala Cys Asn Val Asp His Pro Glu Ile Cys Arg gatgetecag gaccetetga accaegaegt

TABLE 7 DNA Sequence (SEQ ID NO:70) and Protein Sequence (SEQ ID NO:71) of R1.1A

		-														
25	atg Met	ttc Phe	acc Thr	gtg Val	ttt Phe	ctg Leu	ttg Leu	gtt Val	gtc Val	ttg Leu	gca Ala	acc Thr	acc Thr	gtc Val	gtt Val	tcc Ser
														gca Ala		
30	gcg Ala	tct Ser	ggc Gly	ctg Leu	gtc Val	agt Ser	ctg Leu	act Thr	gac Asp	agg Arg	aga Arg	cca Pro	gaa Glu	tgc Cys	tgt Cys	tct Ser
				tgt Cys										tga	agac	get
	gat	gata	cag :	gacc	etet	ga a	ccac	gacg	t							

TABLE 8

DNA Sequence (SEQ ID NO:72) and Protein Sequence (SEQ ID NO:73) of R1.1B 35 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

ttc act tca ggt cgt agt aca ttt cgt ggc agg aat gcc gca gcc aaa Phe Thr Ser Gly Arg Ser Thr Phe Arg Gly Arg Asn Ala Ala Ala Lys gcg tct ggc ctg gtc agt ctg act gac aga aga cca caa tgc tgt tch Ala Ser Gly Leu Val Ser Leu Thr Asp Arg Arg Pro Gln Cys Cys Ser cat cct gcc tgt aac gta gat cat cca gaa att tgc gat tgaagacgct His Pro Ala Cys Asn Val Asp His Pro Glu Ile Cys Asp gatgetccag gaccctctga accagacgt

TABLE 9

DNA Sequence (SEQ ID NO:74) and Protein Sequence (SEQ ID NO:75) of S1.1 atg ttc act gtg ttt ctg ttg gtg atc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala IIe Thr Val Val Ser ttc cct tta gat cgt gas tct gat ggc gcg aat gcc gas gcc Phe Pro Leu Asp Arg Glu Ser Asp Gly Ala Asn Ala Glu Ala Arg Thr cac gat cat gag aag cac gca ctg gac cgg aat ggs tgc tgt agg sat His Asp His Glu Lys His Ala Leu Asp Arg Asn Gly Cys Cys Arg Asn cct gcc tgt gag agc cac aga tgt ggt tgacaget gatgctcag Fro Ala Cys Glu Ser His Arg Cys Gly gaccctctga accacgaget tcgagca

TABLE 10

DNA Sequence (SEQ ID NO:76) and Protein Sequence (SEQ ID NO:77) of Bn1.1 atg ttc acc atg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Met Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc gct tca gat cgt gca tct gat ggc agg aat gcc gca gcc aag gac Phe Ala Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Lys Asp aaa gcg tct gac ctg gct gct ctg acc gtc aag gga tgc tgt tct cat Lys Ala Ser Asp Leu Val Ala Leu Thr Val Lys Gly Cys Cys Ser His cct gcc tgt agc gtg aat act cca gac att tgt ggt tgaagacgct Pro Ala Cys Ser Val Asn Asn Pro Asp Ile Cys Gly gatgctccag gaccctctqa accaqcact tcgagca

TABLE 11

DNA Sequence (SEQ ID NO:78) and Protein Sequence (SEQ ID NO:79) of Bn1.2 aaa gaa tgc tgt act cat cct gcc tgt cac gtg agt cat cca gaa ctc Lys Glu Cys Cys Thr His Pro Ala Cys His Val Ser His Pro Glu Leu tgt ggt tgaaaagcga cgtgacgctc caggacctc tgaaccacga cgttcgagca Cys Gly

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	DNA	A Seq	uenc	e (SE	Q ID	NO:	80) a	nd P	roteir	ı Seq	uence	e (SE	Q ID	NO:	81) c	of Bn1.3	3
	atg Met	ttc Phe	acc Thr	gtg Val	ttt Phe	ctg Leu	ttg Leu	gtt Val	gtc Val	ttg Leu	gca Ala	act Thr	gct Ala	gtt Val	ctt Leu	cca Pro	
5	gtc Val	act Thr	tta Leu	gat Asp	cgt Arg	gca Ala	tct Ser	gat Asp	gga Gly	agg Arg	aat Asn	gca Ala	gca Ala	gcc Ala	aac Asn	gcc Ala	
	aaa Lys	acg Thr	cct Pro	ege Arg	ctg Leu	atc Ile	gcg Ala	cca Pro	ttc Phe	atc Ile	agg Arg	gat Asp	tat Tyr	tgc Cys	tgt Cys	cat His	
10	aga Arg	ggt Gly	ccc Pro	tgt Cys	atg Met	gta Val	tgg Trp	tgt Cys	ggt Gly	tga	agcc	gct	gctg	ctcc	ag		
	gac	ecte	tga .	acca	2												

TABLE 13

DNA Sequence (SEQ ID NO:82) and Protein Sequence (SEQ ID NO:83) of Ca1.1 $$															
atg	ttc	acc	gtg	ttt	ctg	ttg	gtt	gtc	ttg	gca	acc	act	gtg	gtt	tcc
Met	Phe	Thr	Val	Phe	Leu	Leu	Val	Val	Leu	Ala	Thr	Thr	Val	Val	Ser
ttc	act	tca	gat	cgt	gct	tct	gat	ggc	agg	aat	gcc	gca	gcc	aac	gcg
Phe	Thr	Ser	Asp	Arg	Ala	Ser	Asp	Gly	Arg	Asn	Ala	Ala	Ala	Asn	Ala
ttt	gac	ctg	atc	gct	ctg	atc	gcc	agg	caa	aat	tgc	tgt	agc	att	ccc
Phe	Asp	Leu	Ile	Ala	Leu	Ile	Ala	Arg	Gln	Asn	Cys	Cys	Ser	Ile	Pro
agc Ser	tgt Cys	tgg Trp	gag Glu	aaa Lys	tat Tyr	aaa Lys	tgt Cys	agt Ser	taa						

TABLE 14

	DNA Sequence (SEQ I	D NO:84) and Pr	rotein Sequence (SE	Q ID NO:85) of Ca1.2
25	atg ttc acc gtg tt	t ctg ttg gtt	gtc ttg gca acc	act gtg gtt tcc
	Met Phe Thr Val Ph	e Leu Leu Val	Val Leu Ala Thr	Thr Val Val Ser
	ttc act tca gat cg	t gog tot gaa	gge agg aat get	gca gcc aag gac
	Phe Thr Ser Asp Ar	g Ala Ser Glu	Gly Arg Asn Ala	Ala Ala Lys Asp
30	aaa gog tot gao ot	g gtg gct ctg	aca gtc agg gga	tgc tgt gcc att
	Lys Ala Ser Asp Le	u Val Ala Leu	Thr Val Arg Gly	Cys Cys Ala Ile
	cgt gaa tgt cgc tt	g cag aat gca	gcg tat tgt ggt	gga ata tac
	Arg Glu Cys Arg Le	u Gln Asn Ala	Ala Tyr Cys Gly	Gly Ile Tyr
	tgatgctcca ggaccctctg aaccacgacg			

TABLE 15

DNA Sequence (SEQ ID NO:86) and Protein Sequence (SEQ ID NO:87) of TIB atg ttc acc gtg ttt ctg ttg gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

ttc cct tca gat att gca act gag ggc agg aat gcc gca gcc aaa gcg Phe Pro Ser Asp Ile Ala Thr Glu Gly Arg Asn Ala Ala Ala Ala Lys Ala ttt gac ctg ata tct tcg atc gtc aag aaa gga tgc tgt tcc cat cct Phe Asp Leu Ile Ser Ser Ile Val Lys Lys Gly Cys Cys Ser His Pro gcc tgt tcg ggg aat aat cca gaa ttt tgt cgt caa ggt cgc Ala Cys Ser Gly Asn Asn Pro Glu Phe Cys Arg Gln Gly Arg tgatgctcca ggaccctctg aaccacgacg t

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TABLE 16

DNA Sequence (SEQ ID NO:88) and Protein Sequence (SEQ ID NO:89) of TIA atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc cct tca gat ata gca act gag gca gcg gcg gcc aaa gcg Phe Pro Ser Asp Tie Ala Thr Glu Gly Arg Asn Ala Ala Ala Lys Ala ttt gac ctg ata tct tcg atc gtc agg aaa gga tgc tgt tcc aat ccc Phe Asp Leu Ile Ser Ser Ile Val Arg Lys Gly Cys Cys Ser Asn Pro gcc tgt gcg ggg aat aat cca cat gtt tgt cgt caa ggt cgc Ala Cys Ala Gly Asn Asn Pro His Val Cys Arg Gln Gly Arg tgatgctcca ggaccctctg aaccacacac t

TABLE 17

DNA Sequence (SEQ ID NO:90) and Protein Sequence (SEQ ID NO:91) of SI1.1 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc aat tca gat cgt gat cca gca tta ggt ggc agg aat gct gca gcc Phe Asn Ser Asp Arg Asp Pro Ala Leu Gly Gly Arg Asn Ala Ala Ala aaa gcg tct gac aag atc gct tcg acc ctc aag aga aga gga tgc tgt Lys Ala Ser Asp Lys Ile Ala Ser Thr Leu Lys Arg Arg Gly Cys Cys tcg tat ttt gac tgt aga atg atg ttt cca gaa atg tgt ggt tgg cga Ser Tyr Phe Asp Cys Arg Met Met Phe Pro Glu Met Cys Gly Trp Arg ggc tgatgctcca ggaccctctg aaccacgacg t

TABLE 18

DNA Sequence (SEQ ID NO:92) and Protein Sequence (SEQ ID NO:93) of SI1.2 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc aat tca gat cgt gat cca gca tta ggt ggc agg aat gct gca gcc Phe Asn Ser Asp Arg Asp Pro Ala Leu Gly Gly Arg Asn Ala Ala Ala at a gcg tct gac aag atc gct tcg acc ctc agg aga gga gga tgc tgt lie Ala Ser Asp Lys Ile Ala Ser Thr Leu Arg Arg Gly Gly Cys Cys

tot tit oot goo tgt aga aag tat ogt ooa gaa atg tgt ggt gga oga Ser Phe Pro Ala Cys Arg Lys Tyr Arg Pro Glu Met Cys Gly Gly Arg coc tratrictica graccototy aaccacgacy t Arq

TABLE 19

DNA Sequence (SEQ ID NO:94) and Protein Sequence (SEQ ID NO:95) of S11.3 atg tte ace gtg ttt ctg ttg gtt gte ttg gca ace ace gte gtt tee Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser tto act toa gat cat gaa tot gat ogo ggt gat goo caa acc ato caa Phe Thr Ser Asp His Glu Ser Asp Arg Gly Asp Ala Gln Thr Ile Gln gaa gtg ttt gag atg ttc gct ctg gac agc gat gga tgc tgt tgg cat Ğlu Val Phe Ğlu Met Phe Ala Leu Asp Ser Asp Gly Cys Cys Trp His eet get tgt gge aga eac tat tgt ggt ega aga ege tgatgeteea Pro Ala Cys Gly Arg His Tyr Cys Gly Arg Arg Arg

ggaccetetg aaccacgacg t

TABLE 20

DNA Sequence (SEQ ID NO:96) and Protein Sequence (SEQ ID NO:97) of S11.6

atq ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc aat tca gat cgt gat cca gca tta ggt ggc agg aat gct gca gcc Phe Asn Ser Asp Arg Asp Pro Ala Leu Gly Gly Arg Asn Ala Ala Ala ata gog tot gac aag atc got tog acc otc agg aga gga tgo tgt Ile Ala Ser Asp Lys Ile Ala Ser Thr Leu Arg Arg Gly Gly Cys Cys tot tit got god tgt aga aag tat ogt oca gaa atg tgt ggt gga oga Ser Phe Ala Ala Cys Arg Lys Tyr Arg Pro Glu Met Cys Gly Gly Arg

ege tgatget Arg

TABLE 21

DNA Sequence (SEQ ID NO:98) and Protein Sequence (SEQ ID NO:99) of S11.7

atg ttc acc gtg ttt ctg ttg gtt ctc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Leu Leu Ala Thr Thr Val Val Ser ttc aat tca gat cgt gca tta ggt ggc agg aat gct gca gcc aaa gcg Phe Asn Ser Asp Arg Ala Leu Gly Gly Arg Asn Ala Ala Ala Lys Ala tot gac aag atc ott tog aac otc agg aga gga gga tgo tgt ttt cat Ser Asp Lys Ile Leu Ser Asn Leu Arg Arg Gly Gly Cys Cys Phe His cet gtc tgt tac atc aat ctt cta gaa atg tgt cgt caa cga ggc

Pro Val Cys Tyr Ile Asn Leu Leu Glu Met Cys Arg Gln Arg Gly

tgatcgtcca ggaccctctg aaccacgacg t

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TABLE 22

	DNA Sequence (SEQ ID NO:100) and Protein Sequence (SEQ ID NO:101) of Cn1.1 $$	
	atg ttc acc gtg ttt ctg ttg gtt gtc ttg aca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Thr Thr Thr Val Val Ser	
5	tto oot toa gat agt goa tot gat gto agg gat gao gaa goo aaa gao Phe Pro Ser Asp Ser Ala Ser Asp Val Arg Asp Asp Glu Ala Lys Asp	
	gaa agg tot gac atg tac aaa tog aaa ogg aat gga ogo tgt tgo cat Glu Arg Ser Asp Met Tyr Lys Ser Lys Arg Asn Gly Arg Cys Cys His	
10	cct gcc tgt ggc aaa cac ttt agt tgt gga cgc tgatgeteca ggaccetetg Pro Ala Cys Gly Lys His Phe Ser Cys Gly Arg	
	aaccacgacg t	
	TABLE 23	
	DNA Sequence (SEQ ID NO:102) and Protein Sequence (SEQ ID NO:103) of SmI	
15	atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser	
	toe oot toa gat ogt goa tot gat ggo agg aat goo goa goo aac gag Ser Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Glu	
	aaa gog tot gac gtg ato gog otg goo oto aag gga tgo tgt too aac Lys Ala Ser Asp Val Ile Ala Leu Ala Leu Lys Gly Cys Cys Ser Asn	
20	cct gtc tgt cac ctg gag cat tca aac atg tgt ggt aga aga cgc Pro Val Cys His Leu Glu His Ser Asn Met Cys Gly Arg Arg Arg	
	tgatgctcca ggaccctctg aaccacgacg	
	TABLE 24	
	DNA Sequence (SEQ ID NO:104) and Protein Sequence (SEQ ID NO:105) of Bt1.1	
25	atg ttc tcc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Ser Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser	
	tcc act tca ggt ggt gca tct ggt ggc agg aag gct gca gcc aaa gcg Ser Thr Ser Gly Gly Ala Ser Gly Gly Arg Lys Ala Ala Ala Lys Ala	
30	tot aac ogg ato got otg aco gto agg agt goa aca tgo tgt aat tat Ser Asn Arg Ile Ala Leu Thr Val Arg Ser Ala Thr Cys Cys Asn Tyr	
	oct occ tgt tac gag act tat oca gaa agt tgt otg taacgtgaat Pro Pro Cys Tyr Glu Thr Tyr Pro Glu Ser Cys Leu	
	catccagage tttgtggctg aagacactga tgctccagga ccctctgaac cacgacgt	

TABLE 25

DNA Sequence (SEQ ID NO:106) and Protein Sequence (SEQ ID NO:107) of Btl.2

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtg gtt tcc

Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

ttc act tca ggt cgt gca ttt cgt ggc agg aat cgc gca gcc gac gac Phe Thr Ser Gly Arg Ala Phe Arg Gly Arg Asn Arg Ala Ala Asp Asp aaa aagg tct gac ctg gcc gct ctg agc gtc agg gga gga tgc tgt tcc Lys Arg Ser Asp Leu Ala Ala Leu Ser Val Arg Gly Gly Cys Cys Ser cat cct gcc tgt gcg gga aat cat cca gac tt tgt ggc tgaagacgct Ris Pro Ala Cys Ala Val Asn His Pro Glu Leu Cys Gly gatgcccag gaccctctga accacgacgt

TABLE 26

DNA Sequence (SEQ ID NO:108) and Protein Sequence (SEQ ID NO:109) of Bt1.3 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca ggt cgt gca tct ggt ggc agg aat gct gca gcc aaa gcg Phe Thr Ser Gly Arg Ala Ser Gly Gly Arg Asn Ala Ala Ala Lys Ala tct aac cgg atc gct atg gcc atc agc gat gga gca tgc tg gca tat Ser Asn Arg Ile Ala Met Ala Ile Ser Ser Gly Ala Cys Cys Ala Tyr cct ccc tgt ttc gag gct tat cca gaa aga tgt ctg taacgtgaat Pro Pro Cys Phe Glu Ala Tyr Pro Glu Arg Cys Leu catccagacc tttgtggctg aagacgctga tgccccagga ccctctgaac cacgacgt

TABLE 27

DNA Sequence (SEQ ID NO:110) and Protein Sequence (SEQ ID NO:111) of Bt1.4 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca gat cgt gca ttt cgt ggc agg aat tcc gca gcc aac gac Phe Thr Ser Asp Arg Ala Phe Arg Gly Arg Asn Ser Ala Ala Asn Asp aaa agg tct gac ctg gcc gct ctg agc gtc agg aga gga tgc tgc tcc Lys Arg Ser Asp Leu Ala Ala Leu Ser Val Arg Arg Gly Cys Cys Ser cat ccc gcc tgt agc gtg aat cat ca gag ctt tgt ggt aga aga cgc His Pro Ala Cys Ser Val Asn His Pro Glu Leu Cys Gly Arg Arg Arg tgatgccca ggaccctctg aaccacgacg t

TABLE 28

DNA Sequence (SEQ ID NO:112) and Protein Sequence (SEQ ID NO:113) of Btl.5 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca ggt cgt gca tct ggt ggc agg aat gct gca gcc aaa gcg Phe Thr Ser Gly Arg Ala Ser Gly Gly Arg Asn Ala Ala Ala Lys Ala tct aac cgg atc gct ctg atc gtc agg aat gca gaa tgc tgt tat tat Ser Asn Arg Ile Ala Leu Ile Val Arg Asn Ala Glu Cys Cys Tyr Tyr

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cet eec tgt tae gag get tat eea gaa att tgt etg taacgtgaat Pro Pro Cys Tyr Glu Ala Tyr Pro Glu Ile Cys Leu catecagaee tttgtggetg aagaecetga tgeteeagga eectetgaac eacgaegt

TABLE 29

DNA Sequence (SEQ ID NO:114) and Protein Sequence (SEQ ID NO:115) of Pn1.1 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc att tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Ile Ser ttc act tca gat cgt gca tct gat gcc gcg aat gcc gca gcg tct gac Phe Thr Ser Asp Arg Ala Ser Asp Gly Gly Asn Ala Ala Ala Ser Asp ctg atc gct ctg acc atc aag gga tgc tgt tct cat cct ccc tgt gcc Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser His Pro Pro Cys Ala atg aat aat cca gac tat tgt ggt tgacgacgct gatgctccag gaccctctga Met Asn Asn Pro Asp Tyr Cys Gly accacgacg

TABLE 30

DNA Sequence (SEQ ID NO:116) and Protein Sequence (SEQ ID NO:117) of Pn1.2 atg ttc acc gtg ttt ctg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca gat cgt gca tct gat ggc ggg aat gcc gca atg tct gac Phe Thr Ser Asp Arg Ala Ser Asp Gly Gly Asn Ala Ala Met Ser Asp ctg atc gct ctg acc atc aag gga tgc tgt tct cat cct ccc tgt ttc Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser His Pro Pro Cys Phe ctg act act cat gac tat tgt ggt tgacgacgct gatgctccag gaccctctga Leu Asn Asn Pro Asp Tyr Cys Gly accacgacg

TABLE 31

DNA Sequence (SEQ ID NO:118) and Protein Sequence (SEQ ID NO:119) of Sm1.3

atg tto acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc cct tca gat cgt gaa tct gat ggc gcg aat gac gaa gcc cgc acc Phe Pro Ser Asp Arg Glu Ser Asp Gly Ala Asn Asp Glu Ala Arg Thr gac gag cct gag gac cac gga ccg gac agg aat gga tgc tgt agg aat Asp Glu Pro Glu Glu His Gly Pro Asp Arg Asn Gly Cys Cys Arg Asn cct gcc tgt gag agc cac aga tgt ggt tgacgacgct gatgctccag

Pro Ala Cys Glu Ser His Arg Cys Gly

gaccetetga accaegacg

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TABLE 32

DNA Sequence (SEQ ID NO:120) and Protein Sequence (SEQ ID NO:121) of Cr1.2 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

tto cot toa gat ogt goa tot gat ggo agg aat goo goa goo ago gac

Phe Pro Ser Āsp Arg Āla Ser Āsp Gly Arg Asn Ala Ala Ala Ser Asp aga gog tot gac gog goc cac cag gga tgc tgt toc aac cot gto tgt

Arg Ála Ser Ásp Ála Ála His Glí Glý Cýs Cýs Ser Asn Pro Val Cýs cac gtg gas cat cca gas ctt tgt cgt aga aga cgc tgatgctcca

His Val Glu His Pro Glu Leu Cys Arg Arg Arg

ggaccetetg aaccaegaeg

TABLE 33

DNA Sequence (SEQ ID NO:122) and Protein Sequence (SEQ ID NO:123) of Cr1.3

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

tto cot toa aat ogt gaa tot gat ggo gog aat goo gaa gto ogo acc Phe Pro Ser Asn Arg Glu Ser Asp Gly Ala Asn Ala Glu Val Arg Thr

gac gag cct gag gag cac gac gaa ctg ggc ggg aat gga tgc tgt ggg Asp Glu Pro Glu Glu His Asp Glu Leu Gly Gly Asn Gly Cys Cys Gly

aat cet gae tgt aeg age ea
e agt tgt gat tgaegaeget gatgeteeag As
n Pro Asp Cys Thr Ser His Ser Cys Asp $\,$

gaccetetga accaegaeg

TABLE 34

DNA Sequence (SEQ ID NO:124) and Protein Sequence (SEQ ID NO:125) of EpI

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

ttc act tca gat cgt gca tct gat agc agg aag gac gca gcg tct ggc Phe Thr Ser Asp Arg Ala Ser Asp Ser Arg Lys Asp Ala Ala Ser Gly

ctg atc gct ctg acc atc aag gga tgc tgt tct gat cct cgc tgt aac Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser Asp Pro Arg Cys Asn

atg aat aat cca gac tat tg
t ggt tgacgacget gatgetecag gaccetetga Met Asn Asn Pro Asp Tyr Cys Gl
y $\,$

accacgacg

TABLE 35

35 DNA Sequence (SEQ ID NO:126) and Protein Sequence (SEQ ID NO:127) of Sn1.1

atg tcc acc gtg ttt ctg ttg gtt gtc ctc gca acc acc gtc gtt tcc Met Ser Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act gta gat cgt gca tot gat ggc agg gat gtc gca atc gac gac Phe Thr Val Asp Arg Ala Ser Asp Gly Arg Asp Val Ala Ile Asp Asp aga ttg gtg tct ctc cct cag atc gcc cat gct gac tgt tgt tcc gat Arg Leu Val Ser Leu Pro Gln Ile Ala His Ala Asp Cys Cys Ser Asp cct gcc tgc aag cag acg ccc ggt tgt cgt taaaagacgct gctgctccag Pro Ala Cys Lys Gln Thr Pro Gly Cys Arg

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TABLE 36

DNA Sequence (SEQ ID NO:128) and Protein Sequence (SEQ ID NO:129) of Sn1.2 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gct tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Ala Ser ttc att atc gat gat cca tct gat ggc agg aat att gca gtc gac gac Phe Ile Ile Asp Asp Pro Ser Asp Gly Arg Asn Ile Ala Val Asp Asp agg ggg ct ttc tct acc gct gct gac gac gag att tgc gtg gac gag agg ggt ttc tct cat acc gct gat gac cca Arg Gly Leu Phe Ser Thr Leu Phe His Ala Asp Cys Cys Glu Asn Pro gcc tgt aga cac acg cag ggt tgt tgatctttgt tcttcaaaga cactgctggc Ala Cys Arg His Thr Gln Gly Cys ccaggaccct ctgaaccacg acg

TABLE 37

DNA Sequence (SEQ ID NO:130) and Protein Sequence (SEQ ID NO:131) of Dal.1 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca gat cgt gca ttt cgt ggc agg agg aat gcc gca gcc aaa gag Phe Thr Ser Asp Arg Ala Phe Arg Gly Arg Asn Ala Ala Ala Lys Glu tct ggc ctg gtc ggt ctg acc gac aag acg cga gga tgc tgt tct cat Ser Gly Leu Val Gly Leu Thr Asp Lys Thr Arg Gly Cys Cys Ser His cct gcc tgt aac gta gat cat cca gaa att tgt ggt tgaagacgct Pro Ala Cys Asn Val Asp His Pro Glu Ile Cys Gly gatgetccaq gaccctctga accacgacgt

TABLE 38 DNA Sequence (SEO ID NO:132) and Protein Sequence (SEO ID NO:133) of Da1.2

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca gat ggt gca tct gat gac agg aaa gcc gct gcg tct gac Phe Thr Ser Asp Gly Ala Ser Asp Asp Arg Lys Ala Ala Ala Ser Asp ctg acc act ctg acc atc aag gga tgc tgt tct cgt cct ccc tgt atc Leu Ile Thr Leu Thr Ile Lys Gly Cys Cys Ser Arg Pro Pro Cys Ile

geg aat aat coa gac ttg tgt ggt cga ega ege tgatgeteca ggaccetetg Ala Asn Asn Pro Asp Leu Cys Gly Arg Arg Arg

TABLE 39

DNA Sequence (SEO ID NO:134) and Protein Sequence (SEO ID NO:135) of Da1.3

atg tto acc gtg ttt otg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

toc act toa ggt cgt cgt gca ttt cat ggc agg aat gcc gca gcc aaa Ser Thr Ser Gly Arg Arg Ala Phe His Gly Arg Asn Ala Ala Ala Lys

gcg tot gga ctg gtc ggt ctg act gac agg aga cca caa tgc tgt agt Ala Ser Gly Leu Val Gly Leu Thr Asp Arg Arg Pro Gln Cys Cys Ser

gat cct cgc tgt aac gta ggt cat cca gaa ctt tgt ggt gga aga cgc Asp Pro Arg Cys Asn Val Gly His Pro Glu Leu Cys Gly Gly Arg Arg

tgatgctcca ggaccctctg aaccacaacg t

TABLE 40

DNA Sequence (SEQ ID NO:136) and Protein Sequence (SEQ ID NO:137) of Da1.4

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser tcc act tca ggt cgt gca ttt cat ggc agg aat gcc gca gcc aaa gcc Ser Thr Ser Gly Arq Ala Phe His Gly Arg Asn Ala Ala Ala Lys Ala

tot ggc ctg gtc ggt ctg acc gac aag agg caa gta tgc tgt agt gat Ser Giy Leu Val Gly Leu Thr Asp Lys Arg Gln Val Cys Cys Ser Asp

cct cgc tgt aac gta ggt cat cca gaa att tgt ggt gga aga cgc Pro Arg Cys Asn Val Gly His Pro Glu Ile Cys Gly Gly Arg Arg

tgatgctcca ggaccctctg aaccacgacg t

TABLE 41

DNA Sequence (SEQ ID NO:138) and Protein Sequence (SEQ ID NO:139) of A1.2

atg ttc acc gtg ttt ctg ttg gtt gtc ttg aca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Thr Thr Thr Val Val Ser

ttc cct tca gat agt gca tct ggt ggc agg gat gac gag gcc aaa gac Phe Pro Ser Asp Ser Ala Ser Gly Gly Arg Asp Asp Glu Ala Lys Asp

gaa agg tot gac atg tac gaa ttg aaa ogg aat gga ogo tgt tgc cat Glu Arg Ser Asp Met Tyr Glu Leu Lys Arg Asn Gly Arg Cys Cys His

cet gee tgt ggt ggc aaa tac gtt aaa tgt gga ege tgatgeteea

Pro Ala Cys Gly Gly Lys Tyr Val Lys Cys Gly Arg

ggaccetete gaaccacq

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TABLE 42

DNA Sequence (SEQ ID NO:140) and Protein Sequence (SEQ ID NO:141) of Bul.I atg tt acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc tct aca gat gat gaa tct gat ggc tcg aat gaa gaa ccc agc gcc Phe Ser Thr Asp Asp Glu Ser Asp Gly Ser Asn Glu Glu Pro Ser Ala gac cag act gcc agg tcc tca atg aac agg gcc ctg gat tgc tgt aac Asp Gln Thr Ala Arg Ser Ser Met Asn Arg Ala Pro Gly Cys Cys Asn aat cct gcc tgt gtg aag cac aga tgt gat gacgctgat gctccaggac Asn Pro Ala Cys Val Lys His Arg Cys Gly

cctctgaacc acgacgt

TABLE 43

DNA Sequence (SEQ ID NO:142) and Protein Sequence (SEQ ID NO:143) of Bu1.2

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc tct aca gat gat gat act gat ggc tcg aat gaa gaa ccc agc gcc Phe Ser Thr Asp Asp Glu Ser Asp Gly Ser Asn Glu Glu Pro Ser Ala gac cag gct gcc agg tcc gca atg aac agg ccg cct gga tgc tgt aac Asp Gln Ala Ala Arg Ser Ala Met Asn Arg Pro Pro Gly Cys Cys Asn aat cct gcc tgt gtg aag cac aga tgt ggt gga tgacgtgat gctccaggac Asn Pro Ala Cys Val Lys His Arg Cys Gly Gly cctctgaacc acgacgt

TABLE 44

DNA Sequence (SEQ ID NO:144) and Protein Sequence (SEQ ID NO:145) of Bul.3

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

ttc cct tca gat cgt gac tct gat ggc gcg gat gcc gaa gcc agt gac Phe Pro Ser Asp Arg Asp Ser Asp Gly Ala Asp Ala Glu Ala Ser Asp

gag cct gtt gag ttc gaa agg gac gag aat gga tgc tgt tgg aat cct Glu Pro Val Glu Phe Glu Arg Asp Glu Asn Gly Cys Cys Trp Asn Pro

tcc tgt ccg agg ccc aga tgt aca gga cgc cgc taatgeteea ggaccetetg Ser Cys Pro Arg Pro Arg Cys Thr Gly Arg Arg

aaccacgacg t

TABLE 45

35 DNA Sequence (SEQ ID NO:146) and Protein Sequence (SEQ ID NO:170) of Bul.4

atg ttc acc gtg ttt ctg ttg gtt gtc ttg aca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Thr Thr Thr Val Val Ser ttc cct tca gat cgt gca tct gat ggc agg aat gcc gca gcc aac gac Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Ala Ala Ala Asn Asp aaa gcg tct gac gtg gtc acc gtg gtc ctc aag gga tgc tgt tcc acc Lys Ala Ser Asp Val Val Thr Leu Val Leu Lys Gly Cys Cys Ser Thr cct ccc tgt gct gtg ctg tat tgt ggt aga aga gcc tgatgctcca Pro Pro Cys Ala Val Leu Tyr Cys Gly Arg Arg Arg ggaccctctg aaccacgacg t

TABLE 46

DNA Sequence (SEQ ID NO:148) and Protein Sequence (SEQ ID NO:149) of Dil.1 atg ttc acc gtg ttt ctg ttg gtt gtc ttc gca tcc tct gtc acc tta Met Phe Thr Val Phe Leu Leu Val Val Phe Ala Ser Ser Val Thr Leu gat cgt gca tct tat ggc agg tat gcc tca ccc gtc gac agg gcg tct Asp Arg Ala Ser Tyr Gly Arg Tyr Ala Ser Pro Val Asp Arg Ala Ser gcc ctg atc gct cag gcc atc ctt cga gat tgc tgc tca aat cct cct Ala Leu Ile Ala Gln Ala Ile Leu Arg Asp Cys Cys Ser Asn Pro Pro tgt gcc cat aat aat cca gac tgt cgt taaagacgct gcttgctcca cys Ala His Asn Asn Pro Asp Cys Arg

TABLE 47

DNA Sequence (SEQ ID NO:150) and Protein Sequence (SEQ ID NO:151) of TI gga tgc tgt tct aat cct ccc tgt atc gcg aag aat cca cac atg tgt Gly Cys Cys Ser Asn Pro Pro Cys Ile Ala Lys Asn Pro His Met Cys ggt gga aga cgc tga Gly Gly Arg Arg

TABLE 48 DNA Sequence (SEQ ID NO:152) and Protein Sequence (SEQ ID NO:153) of Cn1.2

atg tto acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc cct tca gat cgt gca tct gat ggc agg aat gcc gca gcc aac gac Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Ala Asa Asp Lys Ala Ser Asp Val Ile Thr Leu Ala Leu Lys Gly Cys Cys Ser Asn cct gtc tgt cac ttg aga cat tca aac ctt ggt gcc ctc aag gat gc tgt tcc aac ctg gcc tc ala gray Cys Cys Ser Asn cct gtc tgt cac ttg gag cat tca aac ctt tgt ggt aga aga cgc Pro Val Cys His Leu Glu His Ser Asn Leu Cys Gly Arg Arg Arg tgatgctcca ggaccctctg aaccacgacg t

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TABLE 49

DNA Sequence (SEQ ID NO:233) and Protein Sequence (SEQ ID NO:234) of Im1.1

tet gat gga aag agt gee geg gee aaa gee aaa eeg tet eac etg aeg Ser Asp Gly Lys Ser Ala Ala Ala Lys Ala Lys Pro Ser His Leu Thr

get eea tte ate agg gae gaa tge tgt tee gat tet ege tgt gge aag

Ala Pro Phe Ile Arg Asp Glu Cys Cys Ser Asp Ser Arg Cys Gly Lys

aac tgt ctt tga Asn Cys Leu

TABLE 50

DNA Sequence (SEQ ID NO:235) and Protein Sequence (SEQ ID NO:236) of Im1.2 10

> ttt gat gga agg aat gee eea gee gae gae aaa geg tet gae etg ate Phe Asp Gly Arg Asn Ala Pro Ala Asp Asp Lys Ala Ser Asp Leu Ile

> get caa ate gte agg aga gea tge tgt tee gat egt ege tgt aga tgg

Ala Gln Ile Val Arg Arg Ala Cys Cys Ser Asp Arg Arg Cys Arg Trp

agg tgt ggt tga

Arg Cys Gly

TABLE 51

DNA Sequence (SEQ ID NO:237) and Protein Sequence (SEQ ID NO:238) of Rg1.2

tet gat gga agg aat gee gea gee gae gee aga geg tet eee egg ate Ser Asp Gly Arg Asn Ala Ala Ala Asp Ala Arg Ala Ser Pro Arg Ile

get ett tte etc agg tte aca tgc tgt agg aga ggt ace tgt tee cag Ála Leu Phe Leu Arg Phe Thr Cys Cys Arg Arg Gly Thr Cys Ser Gln

cac tgt ggt tgaagacact gctgctccag gaccctctga accacgacgt His Cvs Glv

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TABLE 52

DNA Sequence (SEQ ID NO:239) and Protein Sequence (SEQ ID NO:240) of Rg1.6

tot aat gga agg aat goo goo goo goo aaa gog tot caa ogg ato Ser Asn Gly Arg Asn Ala Ala Ala Asp Ala Lys Ala Ser Gln Arg Ile

get eea tte ete agg gae tat tge tgt agg aga eat gee tgt aeg ttg Ala Pro Phe Leu Arg Asp Tyr Cys Cys Arg Arg His Ala Cys Thr Leu

att tgt ggt tgaagacget getgeteeag gaecetetga accaegaegt

Ile Cvs Glv

TABLE 53

DNA Sequence (SEQ ID NO:241) and Protein Sequence (SEQ ID NO:242) of Rg1.6A

tot aat gga agg aat goo goo goo goo aaa gog tot caa ogg ato

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Ser Asn Gly Arg Asn Ala Ala Ala Asp Ala Lys Ala Ser Gln Arg Ile got oca tto oto agg gac tat tgo tgt agg aga cot oco tgt acg ttg Ala Pro Phe Leu Arg Asp Tyr Cys Cys Arg Arg Pro Pro Cys Thr Leu att tgt ggt tgaagacgot gctgctocag gaccotctga accacgacgt Ile Cys Gly

TABLE 54

DNA Sequence (SEQ ID NO:243) and Protein Sequence (SEQ ID NO:244) of Rg1.7 tot aat aaa agg aag aat goo goa atg oft gad atg atc got caa cac Ser Asn Lys Arg Lys Asn Ala Ala Met Leu Asp Met Ile Ala Gln His goo ata agg ggt tgc tgt tcc gat cct cgc tgt aga tat aga tgt cgt Ala Ile Arg Gly Cys Cys Ser Asp Pro Arg Cys Arg Tyr Arg Cys Arg tgaagacgct gotgotocag gaccototga accacagacgt

TABLE 55

DNA Sequence (SEQ ID NO:245) and Protein Sequence (SEQ ID NO:246) of Rg1.9

ttt aat gga agg agt gee gee gee gee ea aat geg eet gge etg ate Phe Asn Gly Arg Ser Ala Ala Ala Asp Gln Asn Ala Pro Gly Leu Ile get eaa gte gte aga gga ggg tge tgt tee gat eee ege tge gee tgg Ala Gln Val Val Arg Gly Gly Cys Cys Ser Asp Pro Arg Cys Ala Trp aga tgt ggt tgaagaegtt getgeteeag gaecetetga accaegaegt Arg Cys Gly

TABLE 56

DNA Sequence (SEQ ID NO:247) and Protein Sequence (SEQ ID NO:248) of Rg1.10

ttt gat gga agg aat goc goa goc gac goc aaa gtg att aac acg gtc Phe Asp Gly Arg Asn Ala Ala Ala Asp Ala Lys Val Ile Asn Thr Val got oga atc goc tgg gat ata tgc tgt toc gaa cot gac tgt aac cat Ala Arg Ile Ala Trp Asp Ile Cys Cys Ser Glu Pro Asp Cys Asn His aaa tgt gtt tgaagacget totgotocag gaccototga accacgacgt Lys Cys Val

TABLE 57

30 DNA Sequence (SEQ ID NO:249) and Protein Sequence (SEQ ID NO:250) of Rg1.11 tot aat aaa agg aag aat goo goa atg ott gac atg atc got caa cac

Ser Asn Lys Arg Lys Asn Āla Āla Met Leu Ásp Met Ile Āla Gln His gcc ata agg ggt tgc tgt tcc gat cct cgc tgt aaa cat cag tgt ggt Ala Ile Arg Gly Cys Cys Ser Asp Pro Arg Cys Lys His Gln Cys Gly

tgaagacget getgeteeag gaccetetga accaegaegt

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TABLE 58

DNA Sequence (SEQ ID NO:251) and Protein Sequence (SEQ ID NO:252) of Ms1.7

atc aag aat aca gca gcc agc aac aaa gcg tct agc ctg gtg gct ctt Ile Lys Asn Thr Ala Ala Ser Asn Lys Ala Ser Ser Leu Val Ala Leu gtt gtc agg gga tgc tgt tac aat cct gtc tgc aag aaa tat tat tgt Val Val Arg Gly Cys Cys Tyr Asn Pro Val Cys Lys Lys Tyr Tyr Cys tgg aaa ggc tyatgctca ggaccctctg aaccacgacg t Trp Lys Gly

TABLE 59

DNA Sequence (SEQ ID NO:253) and Protein Sequence (SEQ ID NO:254) of P1.7

tct gaa ggc agg aat gct gaa gcc atc gac aac gcc tta gac cag agg Ser Glu Gly Arg Asn Ala Glu Ala Ile Asp Asn Ala Leu Asp Gln Arg gat cca aag cga cag gag ccg ggg tgc tgt agg cat cct gcc tgt ggg Asp Pro Lys Arg Gln Glu Pro Gly Cys Cys Arg His Pro Ala Cys Gly aag aac aga tgt gga aga cgc tgatgctcca ggaccctctg aaccacgacg t Lys Asn Arg Cys Gly Arg Arg

TABLE 60

DNA Sequence (SEO ID NO:255) and Protein Sequence (SEO ID NO:256) of Ms1.2

tot gat ggc agg aat att gca gtc gac aga tag tot ttc tat acg Ser Asp Gly Arg Asn Ile Ala Val Asp Asp Arg Trp Ser Phe Tyr Thr otc ttc cat gct act tgc tgt gcc gat cot gac tgt aga ttc cgg coc Leu Phe His Ala Thr Cys Cys Ala Asp Pro Asp Cys Arg Phe Arg Pro ggt tgt tgatctttgt tottcaaaga cgctgctggc ccaggaccot ctgaaccacg Gly Cys

acgt

TABLE 61

DNA Sequence (SEQ ID NO:257) and Protein Sequence (SEQ ID NO:258) of Ms1.3

atc aag aat act gca gcc agc aac aaa gcg cct agc ctg gtg gct att Ile Lys Asn Thr Ala Ala Ser Asn Lys Ala Pro Ser Leu Val Ala Ile

gec gtc agg gga tgc tgt tac aat cct tcc tgt tgg ccg aaa aca tat Ala Val Arg Gly Cys Cys Tyr Asn Pro Ser Cys Trp Pro Lys Thr Tyr

tgt agt tggaaagget gatgeteeag gaccetetga accaegaegt

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TABLE 62

DNA Sequence (SEO ID NO:259) and Protein Sequence (SEQ ID NO:260) of Ms1.4

tot gat ago agg aat gto goa ato gag gac aga gtg tot gac otg cac Ser Asp Ser Arg Asn Val Ala Ile Glu Asp Arg Val Ser Asp Leu His tot atg tto tto gat gtt tot tgo tgt ago aat oct aco tgt aaa gaa Ser Met Phe Phe Asp Val Ser Cys Cys Ser Asn Pro Thr Cys Lys Glu acg tat ggt tgt tgatogttgg ttttgaagac gotgatgoto caggaccoto Thr Tyr Gly Cys

TABLE 63

DNA Sequence (SEQ ID NO:261) and Protein Sequence (SEQ ID NO:262) of Ms1.5

tct gtt ggc agg aat att gca gtc gac gac aga ggg att ttc tct acg Ser Val Gly Arg Asn Ile Ala Val Asp Asp Arg Gly Ile Phe Ser Thr ctc ttc cat gct cat tgc tgt gcc aat ccc att gtt aa aa acg ccc cteu Phe His Ala His Cys Cys Ala Asn Pro Ile Cys Lys Asn Thr Pro ggt tgt tgatctttgt tcttcaaaga cgctgctggc ccaggaccct ctgaaccacg Gly Cys acgt

TABLE 64

DNA Sequence (SEQ ID NO:263) and Protein Sequence (SEQ ID NO:264) of Ms1.8

tee gat gge agg aat gte gea ate gae gae agg gtg tet gae etg eac Ser Asp Gly Arg Asn Val Ala Ile Asp Asp Arg Val Ser Asp Leu His tet atg ttc tte gat att get tge tgt aac aat cet ace tgt aaa gaa Ser Met Phe Phe Asp Ile Ala Cys Cys Asn Asn Pro Thr Cys Lys Glu acg tat ggt tgt tgategttgg ttttgaagae getgatgete caggaccete Thr Tyr Gly Cys

TABLE 65

DNA Sequence (SEO ID NO:265) and Protein Sequence (SEQ ID NO:266) of Ms1.9

tot gat ggc agg aat gtc goa atc gag gac aga gtg tot gac ctg otc Ser Asp Gly Arg Asn Val Ala Ile Glu Asp Arg Val Ser Asp Leu Leu tot atg otc ttc gat gtt got tgc tgt agc aat oct gtc tgt aag aas Ser Met Leu Phe Asp Val Ala Cys Cys Ser Asn Pro Val Cys Lys Glu acg tat ggt tgt tgatcgttgg ttttgaagac gotgatgoto caggacooto Thr Tyr Gly Cys

35 tgaaccacga cgt

tat gat ggc agg aat gct gcc gcc gac gac aaa gct ttt gac ctg ctg Tyr Asp Gly Arg Asn Ala Ala Ala Asp Asp Lys Ala Phe Asp Leu Leu

get atg acc ata agg gga gga tgc tgt tee tat eet eee tgt ate geg Ala Met Thr Ile Arg Gly Gly Cys Cys Ser Tyr Pro Pro Cys Ile Ala

agt aat cct aaa tgt ggt gga aga cgc tgatgctcca ggaccctctg Ser Asn Pro Lvs Cvs Glv Glv Arg Arg

aaccacaacg t

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à 4.3 B. :

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DNA Sequence (SEQ ID NO:269) and Protein Sequence (SEQ ID NO:270) of Lv1.5

ttt gat ggc agg aat gct gca ggc aac gcc aaa atg tcc gcc ctg atg Phe Asp Gly Arg Asn Ala Ala Gly Asn Ala Lys Met Ser Ala Leu Met

gee etg acc atc agg gga tge tgt tee eat eet gte tgt age geg atg Ala Leu Thr Ile Arg Gly Cys Cys Ser His Pro Val Cys Ser Ala Met

agt cca atc tgt ggc tgaagacgct gatgccccag gaccctctga accacqacqt Ser Pro Ile Cvs Glv

TABLE 68

DNA Sequence (SEQ ID NO:271) and Protein Sequence (SEQ ID NO:272) of Ms1.10

atc and ant get ged get gac and ged tet gac etg etc tet eng Ile Lys Asn Ala Ala Ala Asp Asp Lys Ala Ser Asp Leu Leu Ser Gln

ate gte agg aat get gea tee aat gae aaa ggg tet gae etg atg act Ile Val Arg Asn Ala Ala Ser Asn Asp Lys Gly Ser Asp Leu Met Thr

ctt gcc ctc agg gga tgc tgt aaa aat cct tac tgt ggt gcg tcg aaa Leu Ala Leu Arg Gly Cys Cys Lys Asn Pro Tyr Cys Gly Ala Ser Lys

aca tat tgt ggt aga aga cgc tgatgeteca ggaccetetg aaccacgaeg t Thr Tyr Cys Gly Arg Arg Arg

TABLE 69

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DNA Sequence (SEQ ID NO:273) and Protein Sequence (SEQ ID NO:274) of Om1.1

totgatggca ggaatgccgc agcgtctgac ctgatggat ctg acc atc aag gga Leu Thr Ile Lvs Gly

> tgc tgt tct tat cct ccc tgt ttc gcg act aat cca gac tgt ggt cga Cvs Cvs Ser Tyr Pro Pro Cys Phe Ala Thr Asn Pro Asp Cys Gly Arg

ega ege tgatgeteca ggaccetetg aaccacgaeg t Arg Arg

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TABLE 70

DNA Sequence (SEQ ID NO:275) and Protein Sequence (SEQ ID NO:276) of R1.6

ttt gat ggc agg aat gee gea gee gac tac aaa ggg tet gaa ttg etc Phe Asp Gly Arg Asn Ala Ala Ala Asp Tyr Lys Gly Ser Glu Leu Leu

gct atg acc gtc agg gga gga tgc tgt tcc tat cct ccc tgt atc gca Ala Met Thr Val Arg Gly Gly Cys Cys Ser Tyr Pro Pro Cys Ile Ala

aat aat oot ott tgt got gga aga ogo tga Asn Asn Pro Leu Cys Ala Gly Arg Arg

TABLE 71

DNA Sequence (SEQ ID NO:277) and Protein Sequence (SEQ ID NO:278) of R1.7

ttt gat ggc agg aat gcc gca gcc gac tac aaa ggg tct gaa ttg ctc Phe Asp Gly Arg Asn Ala Ala Ala Asp Tyr Lys Gly Ser Glu Leu Leu

get atg acc gtc agg gga gga tgc tgt tec tat cet ecc tgt atc gca Ala Met Thr Val Arg Gly Gly Cys Cys Ser Tyr Pro Pro Cys Ile Ala

aat aat oot tit tgt got gga aga ogo tga Asn Asn Pro Phe Cys Ala Gly Arg Arg

TABLE 72

DNA Sequence (SEQ ID NO:279) and Protein Sequence (SEQ ID NO:280) of Vr1.1

tet tat gae agg tat gee teg eee gte gae aga geg tet gee etg ate Ser Tvr Asp Arg Tvr Ala Ser Pro Val Asp Arg Ala Ser Ala Leu Ile

gct cag gcc atc ctt cga gat tgc tgt tcc aat cct ccc tgt tcc caa

Ála Gln Ála Ile Leu Arg Ásp Cys Cys Ser Asn Pro Pro Cys Ser Gln aat aat cca gac tgt atg taaagacget gettgeteea ggaccetetg

Asn Asn Pro Asp Cvs Met

aaccacgacg t

TABLE 73

DNA Sequence (SEO ID NO:281) and Protein Sequence (SEQ ID NO:282) of Vr1.2

tet tat gge agg tat gee tea eee gte gae aga geg tet gee etg ate Ser Tyr Gly Arg Tyr Ala Ser Pro Val Asp Arg Ala Ser Ala Leu Ile

get cag gee ate ett ega gat tge tge tee aat eet eet tgt gee eat Ala Gln Ala Ile Leu Arg Asp Cys Cys Ser Asn Pro Pro Cys Ala His

aat aat cca gac tgt cgt taaagacget gettgeteea ggaceetetg Asn Asn Pro Asp Cys Arg

aaccacgacg t

TABLE 74

DNA Sequence (SEC	ID NO:283) an	d Protein Sequence	(SEO II	NO:284	of A1.4

tot gat ggc agg aat goc goa goc aac gac aac ggc tot ggc atg agc Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Ala Ser Gly Met Ser ggc gtg ggc gat gat gat ggc tgt acc aac cot gtc tgt cac gcg gaa Ala Leu Ala Val Asn Glu Cys Cys Thr Asn Pro Val Cys His Ala Glu cat caa gaa ctt tgt gct aga aga cgc tga

His Gln Glu Leu Cys Ala Arg Arg Arg

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TABLE 75

DNA Sequence (SEQ ID NO:285) and Protein Sequence (SEQ ID NO:286) of A1.5

tet gat gge agg aat gee gea gee aac gac aaa geg tet gac gtg ate Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Ala Ser Asp Val Ile aeg etg gee ete aag gga tge tgt tee aac eet gte tgt eac ttg gag Thr Leu Ala Leu Lys Gly Cys Cys Ser Asn Pro Val Cys His Leu Glu cat tea aac ett tgt ggt aga aga ege tga His Ser Asn Leu Cys Gly Arg Arg Arg

TABLE 76

DNA Sequence (SEQ ID NO:287) and Protein Sequence (SEQ ID NO:288) of A1.6

tct gat ggc agg aat gcc gca gcc aac gac aaa gcg tct ggc atg agc Ser Asp Gly Arg Asn Ala Ala Asn Asp Lys Ala Ser Gly Met Ser gcg ctt gcc gtc aat gaa tgc tgt acc aac cct gtc tgt cac gtg gaa Ala Leu Ala Val Asn Glu Cys Cys Thr Asn Pro Val Cys His Val Glu cat caa gaa ctt tgt gct aga aga cgc tga His Gln Glu Leu Cys Ala Arg Arg Arg

TABLE 77

DNA Sequence (SEQ ID NO:289) and Protein Sequence (SEQ ID NO:290) of Af1.1

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca gat cgt gca ttt cgt ggc agg aat gcc gca gcc aas gcr Phe Thr Ser Asp Arg Ala Phe Arg Gly Arg Asn Ala Ala Ala Lys Ala tct ggc ctg gtc ggt ctg acc gac agg caa gag caa gaa tgc tgt tct tat Ser Gly Leu Val Gly Leu Thr Asp Lys Arg Gln Glu Cys Cys Ser Tyr

cct gcc tgt aac cta gat cat cca gaa ctt tgt ggt tgaagacgct Pro Ala Cys Asn Leu Asp His Pro Glu Leu Cys Gly

gatgetecag gaccetetga accaegacgt

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TABLE 78

DNA Sequence (SEQ ID NO:291) and Protein Sequence (SEQ ID NO:292) of Af1.2 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser toe act toa ggt cgt cgt gca ttt cgt ggc agg aat gcc gca gcc aaa Ser Thr Ser Gly Arg Arg Ala Phe Arg Gly Arg Asn Ala Ala Ala Lys geg tot gga etg gte ggt etg act gae agg aga eca gaa tge tgt agt Ala Ser Gly Leu Val Gly Leu Thr Asp Arg Arg Pro Glu Cys Cys Ser gat cot ege tgt aac teg act cat eca gaa ett tgt ggt gga aga ege Asp Pro Arg Cys Asn Ser Thr His Pro Glu Leu Cys Gly Gly Arg Arg

tgatgeteca ggaccetetg aaccacgacg t

TABLE 79

DNA Sequence (SEO ID NO:293) and Protein Sequence (SEO ID NO:294) of Ar1.2

tet gat gge agg aat gee gea gee aac geg ttt gac etg ate gat etg Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Phe Asp Leu Ile Asp Leu acc gcc agg cta aat tgc tgt atg att ccc ccc tgt tgg aag aaa tat Thr Ala Arg Leu Asn Cys Cys Met Ile Pro Pro Cys Trp Lys Lys Tyr gga gac aga tgt agt gaa gta cgc tgatgctcca ggaccctctg aaccacgacg Gly Asp Arg Cys Ser Glu Val Arg

TABLE 80

DNA Sequence (SEQ ID NO:295) and Protein Sequence (SEQ ID NO:296) of Ar1.3

tot gat ggc agg aat goc gca ogc aaa gog ttt ggc tgc tgc gac tta Ser Asp Gly Arg Asn Ala Ala Arg Lys Ala Phe Gly Cys Cys Asp Leu ata ccc tgt ttg gag aga tat ggt aac aga tgt aat gaa gtg cac Ile Pro Cys Leu Glu Arg Tyr Gly Asn Arg Cys Asn Glu Val His

tgatgctcca ggaccctctg aaccacgcga cgt

TABLE 81

DNA Sequence (SEQ ID NO:297) and Protein Sequence (SEQ ID NO:298) of Ar1.4

30 tot gat ggc agc aat gcc gca gcc aac gag ttt gac ctg atc gct ctg Ser Asp Gly Ser Asn Ala Ala Ala Asn Glu Phe Asp Leu Ile Ala Leu acc gcc agg cta ggt tgc tgt aac gtt aca ccc tgt tgg gag aaa tat Thr Ala Arg Leu Gly Cys Cys Asn Val Thr Pro Cys Trp Glu Lys Tyr qqa qac aaa tgt aat gaa gta cgc tgatgettea ggaccetetg aaccaegaeg 35

Gly Asp Lys Cys Asn Glu Val Arg

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TABLE 82

tct gat ggc agg aat gtc gca gca aaa gcg ttt cac cgg atc ggc cgg Ser Asp Gly Arg Asn Val Ala Ala Lys Ala Phe His Arg Ile Gly Arg acc atc agg gat gaa tgc tgt tcc aat cct gcc tgt agg gtg aat aat

Thr Ile Arg Asp Glu Cys Cys Ser Asn Pro Ala Cys Arg Val Asn Asn

cca cac gtt tgt aga cga cgc tgatgctcca ggaccctctg aaccacgacg t $\mbox{\footnotemark}$ Pro His Val Cys Arg Arg Arg

TABLE 83

DNA Sequence (SEQ ID NO:301) and Protein Sequence (SEQ ID NO:302) of Ar1.6

tct gat ggc agg aat gcc gca gcc aac gcg ttt gac ctg atg cct ctg Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Phe Asp Leu Met Pro Leu acc gcc agg cta aat tgc tgt agc att ccc ggc tgt tgg aac gaa tat

Thr Ala Arg Leu Asn Cys Cys Ser Ile Pro Gly Cys Trp Asn Glu Tyr

aaa gac aga tgt agt aaa gta ege tgatgeteea ggaeeetetg aaceaegaeg Lys Asp Arg Cys Ser Lys Val Arg $\,$

TABLE 84

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DNA Sequence (SEQ ID NO:303) and Protein Sequence (SEQ ID NO:304) of Ay1.2

totgatggca ggaatgccgc agccgacgac aaagcgtotg acctggtogc t otg gto

gte agg gga gga tgc tgt tcc cac cct gtc tgt tac ttt aat aat cca Val Arg Gly Gly Cys Cys Ser His Pro Val Cys Tyr Phe Asn Asn Pro

caa atg tgt cgt gga aga cgc tgatgeteca ggaccetetg aaccaegaeg t Gln Met Cys Arg Gly Arg Arg

TABLE 85

DNA Sequence (SEQ ID NO:305) and Protein Sequence (SEQ ID NO:306) of Ay1.3

tetgatggca ggaatgccgc agccgacgac'aaagcgtetg acctggtege t
 etg gcc Leu Ala

gte agg gga gga tgc tgt tcc cac cct gtc tgt aac ttg aat aat cca Val Arg Gly Gly Cys Cys Ser His Pro Val Cys Asn Leu Asn Asn Pro

caa atg tgt cgt gga aga cgc tgatgeteca ggaceetetg aaceaegaeg t ${\tt Gln}$ Met ${\tt Cys}$ Arg ${\tt Gly}$ Arg Arg

TABLE 86

DNA Sequence (SEQ ID NO:307) and Protein Sequence (SEQ ID NO:308) of Bt1.8

ttt ogt ggc agg aat occ goa gcc aac gac aaa agg tot gac otg gcc Phe Arg Gly Arg Asn Pro Ala Ala Asn Asp Lys Arg Ser Asp Leu Ala gct otg agc gtc agg gga tgc tgt toc cat oct gcc tgt agc gtg Ala Leu Ser Val Arg Gly Gly Cys Cys Ser His Pro Ala Cys Ser Val act cat oca gag ott tgt ggc tgaagacgct gatgccccag gaccotctga Thr His Pro Glu Leu Cys Gly accacagacgt

TABLE 87

DNA Sequence (SEQ ID NO:309) and Protein Sequence (SEQ ID NO:310) of Bt1.9 tot gat ggc ggg aat gcc gca gcc aaa gcg tot gac ctg atc gct cag Ser Asp Gly Gly Asn Ala Ala Ala Lys Ala Ser Asp Leu Ile Ala Gln acc atc agg gga gga tgc tgt toc tat cot gcc tgt agc gtg gaa cat Thr Ile Arg Gly Gly Cys Cys Ser Tyr Pro Ala Cys Ser Val Glu His caa gac ctt tgt gat gga aga cgc tgatgctcca ggaccotctg aaccacgacg Gln Asp Leu Cys Asp Gly Arg Arg

TABLE 88

DNA Sequence (SEQ ID NO:311) and Protein Sequence (SEQ ID NO:312) of Cal.3 tot tat ggc agg aat gcc gca gcc aaa gcg ttt gaa gtg agt tgc tgt Ser Tyr Gly Arg Asn Ala Ala Ala Lys Ala Phe Glu Val Ser Cys Cys gtc gtt cgc ccc tgt tgg att cgc tat caa gag gaa tgt ctt gaa gca Val Val Arg Pro Cys Trp Ile Arg Tyr Gln Glu Glu Cys Leu Glu Ala gat ccc agg acc ctc tga Asp Pro Arg Thr Leu

TABLE 89

DNA Sequence (SEQ ID NO:313) and Protein Sequence (SEQ ID NO:314) of Cal.4 tet gat ggc agg aat gcc gca gcc aac gcc ctt gac ctg atc act ctg Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Leu Asp Leu Ile Thr Leu atc gcc agg caa aat tgc tgt agc att ccc ggc tgt tgg gag aaa tat lea Ala Arg Gln Asn Cys Cys Ser Ile Pro Gly Cys Trp Glu Lys Tyr

gga gac aaa tgt agt gaa gta cgc tga Gly Asp Lys Cys Ser Glu Val Arg

TABLE 90

DNA Sequence (SEQ ID NO:315) and Protein Sequence (SEQ ID NO:316) of C1.2 tot gat ggc agg aat gaa gca gcc aac gac gaa gcg tot gac gtg atc ser Asp Gly Arq Asn Glu Ala Ala Asn Asp Glu Ala Ser Asp Val Ile

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gag ctg gcc ctc aag gga tgc tgt tcc aac cct gtc tgt cac ttg gag Glu Leu Ala Leu Lys Gly Cys Cys Ser Asn Pro Val Cys Ris Leu Glu

cat cca aac gct tgt ggt aga aga cgc tgatgctcca ggaccctctg His Pro Asn Ala Cys Gly Arg Arg Arg

aaccacqacq t

TABLE 91

DNA Sequence (SEQ ID NO:317) and Protein Sequence (SEQ ID NO:318) of C1.3

tet gat gge agg aat gee gea gee aac gae aaa geg tet gae etg gte Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Ala Ser Asp Leu Val get etg gee gte agg gga tge tgt tee aac eet ate tgt tae ttt aat Ala Leu Ala Val Arg Gly Cys Cys Ser Asn Pro Ile Cys Tyr Phe Asn aat eea ega att tgt egt gga aga ege tgatgeteea ggaecetetg Asn Pro Arg Ile Cys Arg Gly Arg Arg

aaccacqacg t

t

TABLE 92

DNA Sequence (SEO ID NO:319) and Protein Sequence (SEQ ID NO:320) of Ep1.2

tct cat ggc agg aat gcc gca cgc aaa gcg tct gac ctg atc gct ctg Ser His Gly Arg Asn Ala Ala Arg Lys Ala Ser Asp Leu Ile Ala Leu acc gtc agg gaa tgc tgt tct cag cct ccc tgt cgc tgg aaa cat cca Thr Val Arg Glu Cys Cys Ser Gln Pro Pro Cys Arg Trp Lys His Pro gaa ctt tgt agt tga Glu Leu Cys Ser

TABLE 93

DNA Sequence (SEQ ID NO:321) and Protein Sequence (SEQ ID NO:322) of G1.1

25 tot gat ggc agg aat gac gca gcc aaa gcg ttt gac ctg ata tot tog
Ser Asp Gly Arg Asn Asp Ala Ala Lys Ala Phe Asp Leu Ile Ser Ser
acc gtc aag aaa gga tgc tgt toc cat cot gcc tgt gcg ggg aat aat
Thr Val Lys Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn Asn
caa cat att tgt ggc cga aga cgc tgatgeteca ggaccetetg aaccacgacg
Gln His Ile Cys Gly Arg Arg

TABLE 94

DNA Sequence (SEQ ID NO:323) and Protein Sequence (SEQ ID NO:324) of G1.3

tot gat ggo agg aat goo goa goo aac gao caa gog tot gao otg atg Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Gln Ala Ser Asp Leu Met

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get geg ace gte agg gga tge tgt gee gtt eet tee tgt ege ete egt Ala Ala Thr Val Arg Gly Cys Cys Ala Val Pro Ser Cys Arg Leu Arg

aat cca gac ctt tgt ggt gga gga cgc tgatgctcca ggaccctctg Asn Pro Asp Leu Cvs Glv Glv Glv Arg

aaccacqacq t

TABLE 95

DNA Sequence (SEQ ID NO:325) and Protein Sequence (SEQ ID NO:326) of Im1.3

ctt gat gaa agg aat goc goa goc gac aaa gog tot gac otg atc Leu Asp Glu Arg Asn Ala Ala Ala Asp Asp Lys Ala Ser Asp Leu Ile

get caa ate gte agg aga tge tgt tee cat eet gee tgt aac gtg Ala Gln Ile Val Arg Arg Gly Cys Cys Ser His Pro Ala Cys Asn Val

aat aat cca cac att tgt ggt tga Asn Asn Pro His Ile Cys Gly

TABLE 96

DNA Sequence (SEO ID NO:327) and Protein Sequence (SEQ ID NO:328) of Lv1.2

tot gat gge agg aat act gca gcc aaa gtc aaa tat tot aag acg ccg

Ser Asp Gly Arg Asn Thr Ala Ala Lys Val Lys Tyr Ser Lys Thr Pro

gag gaa tgc tgt ccc aat cct ccc tgt ttc gcg aca aat tcg gat att Glu Glu Cys Cys Pro Asn Pro Pro Cys Phe Ala Thr Asn Ser Asp Ile

tgt ggc gga aga ege tgatgeteca ggaecetetg aaccaegaeg t

Cys Gly Gly Arg Arg

TABLE 97

DNA Sequence (SEO ID NO:329) and Protein Sequence (SEQ ID NO:330) of Lv1.3

tot aat ggo agg aat goo goa goo aaa tto aaa gog oot goo otg atg Ser Asn Gly Arg Asn Ala Ala Ala Lys Phe Lys Ala Pro Ala Leu Met

> aag cgg acc gtc agg gat gct tgc tgt tca gac cct cgc tgt tcc ggg Lys Arg Thr Val Arg Asp Ala Cys Cys Ser Asp Pro Arg Cys Ser Gly

aaa cat caa gac ctg tgt ggc tgaagacgct gatgctccag gaccctctga Lys His Gln Asp Leu Cys Gly

accacqacqt

TABLE 98

DNA Sequence (SEQ ID NO:331) and Protein Sequence (SEQ ID NO:332) of Lv1.4

tct aat ggc agg aat gcc gca gcc aaa ttc aaa gcg cct gcc ctg atg Ser Asn Gly Arg Asn Ala Ala Ala Lys Phe Lys Ala Pro Ala Leu Met

35 gag ctg acc gtc agg gaa gat tgc tgt tca gac cct cgc tgt tcc gtg Glu Leu Thr Val Arg Glu Asp Cys Cys Ser Asp Pro Arg Cys Ser Val

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gga cat caa gac ctg tgt ggc tgaagacgct gatgctccag gaccctctga Gly His Gln Asp Leu Cys Gly

accacgacgt

TABLE 99

5 DNA Sequence (SEQ ID NO:333) and Protein Sequence (SEQ ID NO:334) of Lv1.6

gca ttt gat ggc agg aat gct gca gcc agg gac aaa gcg tcc gag ctg
Ala Phe Asp Gly Arg Asn Ala Ala Ala Ser Asp Lys Ala Ser Glu Leu

atg gct ctg gcc gtc agg gga tgc tgt tcc cat cct gcc tgt gct ggg
Met Ala Leu Ala Val Arg Gly Cys Cys Ser His Pro Ala Cys Ala Gly

agt aat gca cat atc tgt ggc aga aga cgc tgatgctcca ggaccctctg Ser Asn Ala His Ile Cys Gly Arg Arg Arg

aaccacgacg t

TABLE 100

DNA Sequence (SEQ ID NO:335) and Protein Sequence (SEQ ID NO:336) of Lv1.7

tot aat ggc agg aat gcc gca gcc aaa ttc aaa gcg cct gcc ctg atg Ser Asn Gly Arg Asn Ala Ala Ala Lys Phe Lys Ala Pro Ala Leu Met

aag ctg acc gtc agg gag gat tgc tgt tca gac cct cgc tgt tcc gtg Lys Leu Thr Val Arg Glu Asp Cys Cys Ser Asp Pro Arg Cys Ser Val

gga cat caa gac atg tgt ggc tgaagacgct gatgctccag gaccctctga Glv His Gln Asp Met Cvs Glv

atcacgacgt

TABLE 101

DNA Sequence (SEQ ID NO:337) and Protein Sequence (SEQ ID NO:338) of Lv1.8

ttt gaa tgc agg aat gct gca ggc aac gac aaa gcg act gac ctg atg Phe Glu Cys Arg Asn Ala Ala Gly Asn Asp Lys Ala Thr Asp Leu Met

get etg aet gte agg gga tge tgt tee eat eet gee tgt get ggg aat Ala Leu Thr Val Arg Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn

aat cca cat atc tgc ggc tgaagacgct gatgctccag gaccctctga Asn Pro His Ile Cys Gly

accacgacgt

TABLE 102

DNA Sequence (SEQ ID NO:339) and Protein Sequence (SEQ ID NO:340) of Lv1.9

ttt gat ggc agg aac gcc gca gcc aac aac aaa gcg act gat ctg atg Phe Asp Gly Arg Asn Ala Ala Ala Asn Asn Lys Ala Thr Asp Leu Met

gct ctg act gtc aga gga tgc tgt ggc aat cct tca tgt agc atc cat Ala Leu Thr Val Arg Gly Cys Cys Gly Asn Pro Ser Cys Ser Ile His

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att oot tae git tgt aat tagagaeact gatgeteeag gaeeetetga Ile Pro Tyr Val Cys Asn

accacqacgt

aaccacgacg t

TABLE 103

DNA Sequence (SEQ ID NO:341) and Protein Sequence (SEQ ID NO:342) of Lv1.10

tct aat ggc agg aat gcc gca gcc aaa ttc aaa gcg cct gcc ctg atg
Ser Asn Gly Arg Asn Ala Ala Lys Phe Lys Ala Pro Ala Leu Met

aag cgg acc gac agc gaa gaa tgc tgt tta gac tct cgc tgt gcc ggg
Lys Arg Thr Asp Ser Glu Glu Cys Cys Leu Asp Ser Arg Cys Ala Gly

cas cat cas gac ctg tgt ggc gga aga cgc tgatgctcca ggaccctctg
Gln His Gln Asp Leu Cys Gly Gly Arg Arg

TABLE 104

DNA Sequence (SEQ ID NO:343) and Protein Sequence (SEQ ID NO:344) of Mr1.3

tet gat gge agg aat gee gea gee aag gae aaa geg tet gae etg gte Ser Asp Gly Arg Asn Ala Ala Ala Lys Asp Lys Ala Ser Asp Leu Val get etg ace gte aag gga tge tgt tet aat eet eee tgt tae geg aat Ala Leu Thr Val Lys Gly Cys Ser Asn Pro Pro Cys Tyr Ala Asn aat eaa gee tat tgt aat gga aga ege tga Asn Gln Ala Tyr Cys Asn Gly Arg Arg

TABLE 105

DNA Sequence (SEO ID NO:345) and Protein Sequence (SEO ID NO:346) of Mr1.4

tet gat gge agg aat gee gea gee aag gae aa geg tet gae etg gte Ser Asp Gly Arg Asn Ala Ala Ala Lys Asp Lys Ala Ser Asp Leu Val get etg ace gte agg gga tge tgt tet eat eet gee tgt age gtg aat Ala Leu Thr Val Lys Gly Cys Cys Ser His Pro Ala Cys Ser Val Asn

aat cca gac att tgt ggt tga Asn Pro Asp Ile Cys Gly

TABLE 106

30 DNA Sequence (SEQ ID NO:347) and Protein Sequence (SEQ ID NO:348) of Ms1.1

tet gat ggc agg aat get gea gee aac aac aaa gtg get ttg aec atg Ser Asp Gly Arg Asn Ala Ala Ala Asn Asn Lys Val Ala Leu Thr Met agg gga aaa tge tgt ate aat gat geg tgt ege teg aac eat eec eag Arg Gly Lys Cys Cys Ile Asn Asp Ala Cys Arg Ser Lys His Pro Gln

tac tgt tot gga aga ogc tgatactoca ggaccototg aaccacgacg t Tyr Cys Ser Gly Arg Arg tot gat qqc agg aat gct gca gcc aac gac aaa gtg tot gac cag atg Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Val Ser Asp Gln Met

gct ctg gtt gtc agg gga tgc tgt tac aat att gcc tgt aga att aat Ala Leu Val Val Arg Gly Cys Cys Tyr Asn Ile Ala Cys Arg Ile Asn

aat cca cgg tac tgt cgt gga aaa cgc tgatgtteca ggaccetetg Asn Pro Arg Tyr Cys Arg Gly Lys Arg

aaccacgacg t

TABLE 108

DNA Sequence (SEQ ID NO:351) and Protein Sequence (SEQ ID NO:352) of O1.1

tetgaaggea ggaatgeege agecaaegae aaagegtetg acetgatgge t etg aac

gtc agg gga tgc tgt tcc cat cct gtc tgt cgc ttc aat tat cca aaa Val Arg Gly Cys Cys Ser His Pro Val Cys Arg Phe Asn Tyr Pro Lys

tat tot got goa aga cgc tgatggtcca ggaccctctg aaccacgacg t Tyr Cys Gly Gly Arg Arg

TABLE 109

DNA Sequence (SEQ ID NO:353) and Protein Sequence (SEQ ID NO:354) of O1.2

tetgatggeg ggaatgeege ageaaaageg titgatetaa teact etg gee etc agg

gat gaa tgc tgt gcc agt cct ccc tgt cgt ttg aat aat cca tac gta Asp Glu Cys Cys Ala Ser Pro Pro Cys Arg Leu Asn Asn Pro Tyr Val

tat cat tgacgacget gatgetecag gaccetetga accacgacgt Cvs His

TABLE 110

DNA Sequence (SEO ID NO:355) and Protein Sequence (SEO ID NO:356) of O1.4

atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser

ecc act tea gat eqt gea tet gat agg agg aat gee gea gee aaa geg Pro Thr Ser Asp Arg Ala Ser Asp Arg Arg Asn Ala Ala Ala Lys Ala

ttt gae etg aga tat teg ace gee aag aga gga tge tgt tee aat eet Phe Asp Leu Arg Tyr Ser Thr Ala Lys Arg Gly Cys Cys Ser Asn Pro

gto tgt tgg cag aat aat gca gaa tac tgt cgt gaa agt ggc

Val Cys Trp Gln Asn Asn Ala Glu Tyr Cys Arg Glu Ser Gly

taatgeteea ggaccetetg aaccaegaeg t

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								TAB	LE 1	11							
	DNA	Sequ	ience	(SE	Q ID	NO:	357) :	and P	rotei	n Sec	quenc	e (SI	EQ II) NO	:358)	of O1.7	
		ttc Phe															
5		act Thr															
		atc Ile															
10		aat Asn							tgad	gac	gct (gatgo	ctcca	ag ga	ecct	ctga	
	acc	acga	egt														
								TAE	BLE 1	12							
	DNA	Seq	uence	e (SE	Q ID	NO:	359)	and I	rotei	n Se	queno	e (Sl	EQ II	ON C	:360)	of O1.8	
15		ttc Phe															
		act Thr															
		gac Asp															
20	gcc Ala	tgt Cys	tcg Ser	ggg Gly	aat Asn	aat Asn	cga Arg	gaa Glu	tat Tyr	tgt Cys	cgt Arg	gaa Glu	agt Ser	ggc Gly			
	taa	tgct	cca	ggac	cctc	tg a	acca	egae	g t								
								TAI	BLE :	113							
	DNA	Sequ	ence	(SEC	Q ID	NO:3	61) a	nd P	roteii	n Seq	uenc	e (SE	Q ID	NO:	362)	of Om1.2	
25	ttt	gatg	gca	ggaa	tgcc	tc a	gccg	acag	c aa	agtg	gctg	ccc	ggat	cge		g atc n Ile	

DNA Sequence (SEQ ID NO:361) and Protein Sequence (SEQ ID NO:362) of Om1.2

tttgatggca ggaatgcctc agccgacagc aaagtggctg cccggatcgc t cag atc Gln Ile

gac agg gat cca tgc tgt tcc tat cct gac tgt ggc gcg aat cat cca
Asp Arg Asp Pro Cys Cys Ser Tyr Pro Asp Cys Gly Ala Asn His Pro

gag att tgt ggt gga aaa cgc tgatgctcca ggaccctctg aaccacgacg t
Glu Ile Cys Gly Gly Lys Arg

TABLE 114

DNA Sequence (SEQ ID NO:363) and Protein Sequence (SEQ ID NO:364) of Om1.3 teteatggca ggaatgeege aeget etg acc gte agg gaa tge tgt tet eag Leu Thr Val Arg Glu Cys Cys Ser Gln

35 cct cct tgt cgc tgg aaa cat cca gaa ctt tgt agt tgaagacgct Pro Pro Cys Arg Trp Lys His Pro Glu Leu Cys Ser

TABLE 115

<u> </u>
DNA Sequence (SEQ ID NO:365) and Protein Sequence (SEQ ID NO:366) of Oml
tttgatggca ggaatgctgc agccagcgac aaagcgtctg agctgatggc t ctg gcc Leu Ala
gtc agg gga tgc tgt tcc cat cct gcc tgt gct ggg aat aat cca cat Val Arg Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn Asn Pro His
atc tgt ggc aga aga cgc tgatgctcca ggaccctctg aaccacgacg t Ile Cys Gly Arg Arg Arg

	<u>TABLE 116</u>
L	DNA Sequence (SEQ ID NO:367) and Protein Sequence (SEQ ID NO:368) of Om1.5
	totggtgtca ggaaagacgc agcgcctggc ctgatcgct ctg acc atc aag gga $$\operatorname{Leu}$$ The Ile Lys Gly
	tgc tgt tct gat cct agc tgt aac gtg aat aat cca gac tat tgt ggt Cys Cys Ser Asp Pro Ser Cys Asn Val Asn Asn Pro Asp Tyr Cys Gly
	tgacgacgct gatgctccag gaccctctga accacgacgt

TABLE 117 DNA Sequence (SEQ ID NO:369) and Protein Sequence (SEQ ID NO:370) of Om1.6

tctaatggca ggaatgccgc agccaaattc aaagcgcctg ccctgatgga g ctg acc Leu Thr	57				
gtc agg gaa gaa tgc tgt tca gac cct cgc tgt tcc gtg gga cat caa Val Arg Glu Glu Cys Cys Ser Asp Pro Arg Cys Ser Val Gly His Gln	105				
gat atg tgt cgg tgaagcacgt gatgeteeag gaeeetetga accaegaegt Asp Met Cys Arg	157				
TABLE 118					
DNA Sequence (SEQ ID NO:371) and Protein Sequence (SEQ ID NO:372) of P1.4					

act gat ggc agg aat gct gca gcc ata gcg ctt gac ctg atc gct ccg Thr Asp Gly Arg Asn Ala Ala Ala Tie Ala Leu Asp Leu Ile Ala Pro gcc gtc agg gga gga tgt tgt tcc aat cct gcc tgt tta gtg aat cat Ala Val Arg Gly Gly Cys Cys Ser Asn Pro Ala Cys Leu Val Asn His cta gaa atg tgt ggt aaa aga cgc tgatgcccca ggaccctctg aaccacgacg Leu Glu Met Cys Gly Lys Arg Arg

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TABLE 119

DNA Sequence (SEQ ID NO:373) and Protein Sequence (SEQ ID NO:374) of P1.5 tot gat ggc agg gat gcc gca gcc aac gac aaa gcg tot gac otg atc Ser Asp Gly Arg Asp Ala Ala Ala Asa Asp Lys Ala Ser Asp Leu Ille gct ctg acc gcc agg aga gat cca tgc tgt ttc aat cct gcc tgt aac Ala Leu Thr Ala Arg Arg Asp Pro Cys Cys Phe Asa Pro Ala Cys Asa gtg aat aat cca cag att tgt ggt tgaagacgct gatgctccag gaccototga Val Asa Asa Pro Gln Ile Cys Gly

accacgacgt

TABLE 120

DNA Sequence (SEQ ID NO:375) and Protein Sequence (SEQ ID NO:376) of P1.6 tot gat ggc agg gat gct gag aaa aca ggc ttt gac acg acc att gtg Ser Asp Gly Arg Asp Ala Glu Lys Thr Gly Phe Asp Thr Thr Ile Val ccg gaa gac tgc tgt tcg gat cct tcc tgt tgg agg ctg cat agt tta Pro Glu Asp Cys Cys Ser Asp Pro Ser Cys Trp Arg Leu His Ser Leu gct tgt act gga att gta aac cgc tgatgctcca ggaccctctg aaccacgacg Ala Cys Thr Gly Ile Val Asn Arg

TABLE 121

DNA Sequence (SEQ ID NO:377) and Protein Sequence (SEQ ID NO:378) of P1.8 act gat ggc agg agt gct gca gcc ata gcg ttt gcc ctg atc gct ccg Thr Asp Gly Arg Ser Ala Ala Ala Ile Ala Phe Ala Leu Ile Ala Pro acc gtc tgc tgt act aat cct gcc tgt ctc gtg aat aat ata cgc ttt Thr Val Cys Cys Thr Asn Pro Ala Cys Leu Val Asn Asn Ile Arg Phe tgt ggt gga agc cgc tgatgcccca ggaccetctg aaccacgacg t Cys Gly Gly Arg Arg

TABLE 122

DNA Sequence (SEQ ID NO:379) and Protein Sequence (SEQ ID NO:380) of Rg1.1 tot gat gga aga aat goo goo ago goo goo aaa gog ttt coo ogg ato

Ser Ásp ŐÍy Arg Asn Ála Ála Sér Ásp Ála Lys Álá Fhe Pro Arg Ile gct cca atc gtc agg gac gaa tgc tgt agc gat cct agg tgt cac ggg Ala Pro Ile Val Arg Asp Glu Cys Cys Ser Asp Pro Arg Cys His Gly aat aat cgg gac cac tgt gct tgaagacgct gctgctccag gaccetctga Asn Asn Arq Asp His Cys Ala

35 accacgacgt

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00400700	
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DNA Sequence (SEO ID NO:381) and Protein Sequence (SEQ ID NO:382) of Rg1.3

tot gat ggc agg aat acc gcg gcc gac gaa aaa gcg toc gac ctg atc Ser Asp Gly Arg Asn Thr Ala Ala Asp Glu Lys Ala Ser Asp Leu Ile tot caa act gtc aag aga gat tgc tgt toc cat cot otto tgt aga tta Ser Gln Thr Val Lys Arg Asp Cys Cys Ser His Pro Leu Cys Arg Leu ttt gtt coa gga ctt tgt att tgaagacgot gctgctccag gaccotctga Phe Val Pro Gly Leu Cys Ile

accacgact

TABLE 124

DNA Sequence (SEQ ID NO:383) and Protein Sequence (SEQ ID NO:384) of Rg1.4

tct gat ggc agg aat gcc gca gcc gac aac aaa gcg tct gac cta atc Ser Asp Gly Arg Asn Ala Ala Ala Asp Asn Lys Ala Ser Asp Leu Ile gct caa atc gtc agg aga gga tgc tgt tcc cat cct gtc tgt aaa gtg Ala Gln Ile Val Arg Arg Gly Cys Cys Ser His Pro Val Cys Lys Val agg tat cca gac ctg tgt cgt tgaagacgct gctgctccag gaccctctga Arg Tyr Pro Asp Leu Cys Arg

TABLE 125

DNA Sequence (SEQ ID NO:385) and Protein Sequence (SEQ ID NO:386) of Rg1.5

tet gat ggc agg aat gec gea gec gac aac agg geg tet gac eta atc Ser Asp Gly Arg Asn Ala Ala Ala Asp Asn Arg Ala Ser Asp Leu Ile get caa atc gcc agg agga tgg tgt tec cat cet gec tgt aat gtg Ala Gin Ile Val Arg Arg Gly Cys Cys Ser His Pro Ala Cys Asn Val aat aat cca cac att tgt ggt tgaagacget getgetecag gaccetetga Asn Asn Pro His Ile Cys Gly

accacgacgt

TABLE 126

DNA Sequence (SEQ ID NO:387) and Protein Sequence (SEQ ID NO:388) of Rg1.8

tot gat ggc agg aat gcc gca gcc gac aac aaa cog tot gac ota atc Ser Asp Gly Arg Asn Ala Ala Ala Asp Asn Lys Pro Ser Asp Leu Ile gct caa atc gtc agg aga gga tgc tgt tcg cat cot gtc tgt aaa gtg Ala Gln Ile Val Arg Arg Gly Cys Cys Ser His Pro Val Cys Lys Val agg tat tca gac atg tgt ggt tgaagacgct gctgctccag gaccotctga Arg Tyr Ser Asp Met Cys Gly

accacqacqt

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TABLE 127

DNA Sequence (SEQ ID NO:389) and Protein Sequence (SEQ ID NO:390) of Sm1.4

tot gat ggc agg aat goa gag cga cga caa agc gtc tgt cct ggt cgc Ser Asp Gly Arg Asn Ala Glu Arg Arg Gln Ser Val Cys Pro Gly Arg tct ggc ccc agg gga gga tgt tgt tcc cac cct gcc tgt aag gtg cat Ser Gly Pro Arg Gly Gly Cys Cys Ser His Pro Ala Cys Lys Val His ttt coa cac agt tgt ggt tgacgacgct gatgctccag gaccctctga

Phe Pro His Ser Cys Gly

accacgacgt

TABLE 128

DNA Sequence (SEQ ID NO:391) and Protein Sequence (SEQ ID NO:392) of Sm1.5

tot gat ggc agg aat gcc gca gcc agc gac aga gcg tot gac gcg gcc Ser Asp Gly Arg Asn Ala Ala Ala Ser Asp Arg Ala Ser Asp Ala Ala cac cag gta tgc tgt tcc aac cct gtc tgt cac gtg gat cat cca gaa His Gln Val Cys Cys Ser Asn Pro Val Cys His Val Asp His Pro Glu ctt tgt cgt aga aga cgc tgatgctcca ggaccctctg aaccacgacg t Leu Cys Arg Arg Arg

TABLE 129

DNA Sequence (SEQ ID NO:393) and Protein Sequence (SEQ ID NO:394) of S1.5

tet gat gge agg aat gee geg gee aac gac aaa geg tet gac etg gte Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Ala Ser Asp Leu Val get eeg gee ate agg gga tge tgt tee cac eet gte tgt aac ttg agt Ala Pro Ala 11e Arg Gly Cys Cys Ser His Pro Val Cys Asn Leu Ser aat eea caa att tgt egt gga aga ege tgatgeteea ggaccetetg Asn Pro Gln Ile Cys Arg Gly Arg Arg

aaccacgacg t

TABLE 130

DNA Sequence (SEQ ID NO:395) and Protein Sequence (SEQ ID NO:396) of Tx1.5

ttt cat ggc agg aat gcc gca gcc aaa gcg tct ggc ctg gtc ggt ctg Phe His Gly Arg Asn Ala Ala Ala Lys Ala Ser Gly Leu Val Gly Leu acc gac aag agg caa gaa tgc tgt tct cat cct gcc tgt aac gta gat Thr Asp Lys Arg Gln Glu Cys Cys Ser His Pro Ala Cys Asn Val Asp cat cca gaa att tct cgt tga

His Pro Glu Ile Cys Arg

ace qte tgg gaa gga tgc tgt tct aat cct gcc tgt ctc gtg aat cat Thr Val Trp Glu Gly Cys Cys Ser Asn Pro Ala Cys Leu Val Asn His

ata ege ttt tgt ggt gga aga ege tgatgeecca ggaccetetg aaccacqacq Ile Ara Phe Cvs Glv Glv Ara Ara

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TABLE 132

DNA Sequence (SEQ ID NO:399) and Protein Sequence (SEQ ID NO:400) of Vr1.3

tot aat ggc atg aat gee gea gee ate agg aaa geg tot gee etg gtg Ser Asn Gly Met Asn Ala Ala Ala Ile Arg Lys Ala Ser Ala Leu Val

get cag atc gcc cat cga gac tgc tgt gac gat cct gcc tgc acc gtg Ala Gln Ile Ala His Arg Asp Cys Cys Asp Asp Pro Ala Cys Thr Val

aat aat eea ggc ett tge act tgaagatget getgeeceag gaccetetga Asn Asn Pro Gly Leu Cys Thr

accacgacgt

TABLE 133

DNA Sequence (SEO ID NO:401) and Protein Sequence (SEO ID NO:402) of G1.2

tet gat gge ggg aat gee gea gea aaa gag tet gae gtg ate get etg

Ser Āsp Gly Gly Asn Āla Āla Āla Lys Glu Ser Āsp Val Ile Āla Leu

acc gtc tgg aaa tgc tgt acc att cct tcc tgt tat gag aaa aaa aaa Thr Val Trp Lys Cys Cys Thr Ile Pro Ser Cys Tyr Glu Lys Lys Lys

att aaa gca tgt gtc ttt tgacgacgct gatgctccag gaccctctga Ile Lys Ala Cys Val Phe

accacgacgt

TABLE 134

DNA Sequence (SEO ID NO:403) and Protein Sequence (SEQ ID NO:404) of Rg1.12

tet gat gge gea gte gae gae aaa geg ttg gat ega ate get gaa ate Ser Asp Gly Ala Val Asp Asp Lys Ala Leu Asp Arg Ile Ala Glu Ile

gtc agg aga gga tgc tgt ggc aat cct gcc tgt agc ggc tcc tcg aaa Val Arg Arg Gly Cys Cys Gly Asn Pro Ala Cys Ser Gly Ser Ser Lys

gat gca ccc tct tgt ggt tgaagacgct gctgctccag gaccctctga Asp Ala Pro Ser Cys Gly

accacgacgt

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It will be appreciated that the methods and compositions of the instant invention can be incorporated in the form of a variety of embodiments, only a few of which are disclosed herein. It will be apparent to the artisan that other embodiments exist and do not depart from the spirit of the invention. Thus, the described embodiments are illustrative and should not be construed as restrictive.

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PCT Published Application WO 96/11698.

PCT Published Application WO 96/40871.

PCT Published Application WO 96/40959.

PCT Published Application WO 97/12635.

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WHAT IS CLAIMED IS:

- 1. A substantially pure α-conotoxin peptide having the generic formula I: Xaa₁-Xaa₂-Xaa₃-Xaa₄-Xaa₅-Cys-Cys-Xaa₆-Xaa₇-Xaa₈-Xaa₉-Cys-Xaa₁₀-Xaa₁₁-Xaa₁₂-Cys-Xaa₁₃ (SEQ ID NO1:), wherein Xaa, is des-Xaa, Ile, Leu or Val; Xaa, is des-Xaa, Ala or Gly; Xaa, is des-Xaa, Gly, Trp (D or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid; Xaa4 is des-Xaa., Asp. Phe, Gly, Ala, Glu, y-carboxy-Glu (Gla) or any unnatural aromatic amino acid: Xaa, is Glu, Gla, Asp, Ala, Thr, Ser, Gly, Ile, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid: Xaa, is Ser. Thr. Arg. ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid; Xaa₂ is Asp. Glu, Gla, Arg. ornithine, homoarginine, Lvs, N-methyl-Lvs, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₈ is Ser, Thr, Asn, Ala, Gly, His, halo-His, Pro or hydroxy-Pro; Xaa, is Thr, Ser, Ala, Asp, Asn, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lvs. N-methyl-Lvs, N,N-dimethyl-Lvs, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa10 is Gly, Ser, Thr, Ala, Asn, Arg, ornithine, homoarginine, Lvs. N-methyl-Lvs. N.N-dimethyl-Lvs. N.N.-trimethyl-Lvs or any unnatural basic amino acid; Xaa1 is Gln, Leu, His, halo-His, Trp (D or L), halo-Trp, neo-Trp, Tyr, nor-Tyr, monohalo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid or any unnatural aromatic amino acid; Xaa1, is Asn, His, halo-His, Ile, Leu, Val., Gln., Arg., ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,Ntrimethyl-Lys or any unnatural basic amino acid; Xaa,3 is des-Xaa,3 Val, Ile, Leu, Arg, ornithine, homoarginine, Lvs, N-methyl-Lvs, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; and the C-terminus contains a free carboxyl group or an amide group.
- A substantially pure α-conotoxin peptide of generic formula I selected from the group consisting of:

Asp-Xaa₁-Cys-Cys-Ser-Asp-Ser-Arg-Cys-Gly-Xaa₂-Asn-Cys-Leu (SEQ ID NO:4); Ala-Cys-Cys-Ser-Asp-Arg-Arg-Cys-Arg-Xaa₃-Arg-Cys (SEQ ID NO:5); Phe-Thr-Cys-Cys-Arg-Arg-Gly-Thr-Cys-Ser-Gln-His-Cys (SEQ ID NO:6);

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Asp-Xaa₄-Cys-Cys-Arg-Arg-His-Ala-Cys-Thr-Leu-Ile-Cys (SEQ ID NO:7);

Asp-Xaa₄-Cys-Cys-Arg-Xaa₅-Xaa₅-Xaa₇-Cys-Thr-Leu-Ile-Cys (SEQ ID NO:8);

Gly-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Arg-Xaa₄-Arg-Cys-Arg (SEQ ID NO:9);

Gly-Gly-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Ala-Xaa₅-Arg-Cys (SEQ ID NO:10);

Ile-Ala-Xaa₅-Asp-Ile-Cys-Cys-Ser-Xaa₁-Xaa₅-Asp-Cys-Asn-His-Xaa₂-Cys-Val(SEQ

ID NO:11); and

Gly-Cys-Cys-Ser-Asp-Xaa₃-Arg-Cys-Xaa₂-His-Gln-Cys (SEQ ID NO:12), wherein Xaa₁ is Glu or γ -carboxy-Glu (Gla); Xaa₂ is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa₃ is Trp (D or L), halo-Trp or neo-Trp; Xaa₄ is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa₃ is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

- 3. The substanially pure α -conotoxin peptide of claim 2, wherein Xaa $_1$ is Glu.
- 4. The substantially pure α -conotoxin peptide of claim 2, wherein Xaa $_2$ is Lys.
- 5. The substantially pure $\alpha\text{-conotoxin}$ peptide of claim 2, wherein Xaa $_4$ is Tyr.
- The substantially pure α-conotoxin peptide of claim 2, wherein Xaa₄ is mono-iodo-Tyr.
 - 7. The substantially pure α -conotoxin peptide of claim 2, wherein Xaa $_4$ is di-iodo-Tyr.
 - The substantially pure α-conotoxin peptide of claim 1, which is modified to contain an Oglycan, an S-glycan or an N-glycan.
 - 9 The substantially pure α-conotoxin peptide of claim 2 which is modified to contain an O-glycan, an S-glycan or an N-glycan.
 - 10 A substantially pure α-conotoxin peptide having the generic formula II: Xaa₁-Xaa₂-Xaa₃-Xaa₄-Cys-Cys-Xaa₅-Xaa₆-Xaa₁₇-Xaa₁₆-Xaa₁₇-Xaa₁₈-Xaa₁

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Xaa, is des-Xaa, Gln, Ala, Asp, Glu, Gla; Xaa, is des-Xaa, Gly, Ala, Asp, Glu, Gla, Pro or hydroxy-Pro; Xaa4 is des-Xaa4, Gly, Glu, Gla, Gln, Asp, Asn, Pro or hydroxy-Pro; Xaa5 is Ser, Thr, Gly, Glu, Gla, Asn, Trp (D or L), neo-Trp, halo-Trp, Arg, ornithine, homoarginine, Lvs, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tvr or any unnatural hydroxy containing amino acid; Xaa, is Asp, Asn, His, halo-His, Thr, Ser, Tvr, nor-Tvr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa, is Pro or hydroxy-Pro; Xaa, is Ala, Ser, Thr, Asp, Val, Ile, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaao is Gly, Ile, Leu, Val, Ala, Thr, Ser, Pro, hydroxy-Pro, Phe, Trp (D or L), neo-Trp, halo-Trp, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid or any unnatural aromatic amino acid; Xaa10 is Ala, Asn, Phe, Pro, hydroxy-Pro, Glu, Gla, Gln, His, halo-His, Val, Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa11 is Thr, Ser, His, halo-His, Leu, Ile, Val, Asn, Met, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,Ntrimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa12 is Asn, Pro, hydroxy-Pro, Gln, Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa13 is des-Xaa13, Gly, Thr, Ser, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa14 is des-Xaa14, Ile, Val, Asp, Leu, Phe, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, Ophospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; and Xaa15 is des-Xaa15, Gly, Ala, Met, Ser, Thr, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,Ntrimethyl-Lys or any unnatural basic amino acid; Xaa16 is des-Xaa16, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-

Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₇ is des-Xaa₁₇, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; and the C-terminus contains a free carboxyl group or an amide group.

 A substantially pure α-conotoxin peptide of generic formula II selected from the group consisting of:

> Cys-Cys-Ser-Asp-Xaa₃-Ala-Cys-Xaa₂-Gln-Thr-Xaa₅-Gly-Cys-Arg (SEQ ID NO:13); Cys-Cys-Xaa₁-Asn-Xaa₃-Ala-Cys-Arg-His-Thr-Gln-Gly-Cys (SEQ ID NO:14); Gly-Cys-Cys-Xaa₃-His-Xaa₅-Ala-Cys-Gly-Arg-His-Xaa₄-Cys (SEQ ID NO:15); Ala-Xaa₅-Cys-Cys-Asn-Asn-Xaa₅-Ala-Cys-Val-Xaa₂-His-Arg-Cys (SEQ ID NO:16); Ala-Xaa₅-Gly-Cys-Cys-Asn-Asn-Xaa₅-Ala-Cys-Val-Xaa₂-His-Arg-Cys (SEQ ID NO:17);

> Xaa₃-Xaa₃-Cys-Cys-Asn-Asn-Xaa₃-Ala-Cys-Val-Xaa₂-His-Arg-Cys (SEQ ID NO:18);

Asp-Xaa₁-Asn-Cys-Cys-Xaa₃-Asn-Xaa₅-Ser-Cys-Xaa₅-Arg-Xaa₅-Arg-Cys-Thr(SEQ ID NO:19);

Gly-Cys-Cys-Ser-Thr-Xaa₃-Xaa₃-Cys-Ala-Val-Leu-Xaa₄-Cys (SEQ ID NO:20); Gly-Cys-Gly-Asn-Xaa₃-Asp-Cys-Thr-Ser-His-Ser-Cys (SEQ ID NO:21); Gly-Cys-Cys-Ser-Asn-Xaa₃-Xaa₃-Cys-Ala-His-Asn-Asn-Xaa₃-Asp-Cys-Arg (SEQ ID NO:42);

 $Gly-Cys-Cys-Xaa_4-Asn-Xaa_5-Val-Cys-Xaa_2-Xaa_2-Xaa_4-Xaa_4-Cys-Xaa_3-Xaa_2 (SEQ\ ID\ NO:154);$

Xaa₆-Xaa₃-Xaa₅-Gly-Cys-Cys-Arg-His-Xaa₅-Ala-Cys-Gly-Xaa₂-Asn-Arg-Cys (SEQ ID NO:155):

Cys-Cys-Ala-Asp-Xaa₅-Asp-Cys-Arg-Phe-Arg-Xaa₅-Gly-Cys (SEQ ID NO:156); Gly-Cys-Cys-Xaa₄-Asn-Xaa₅-Ser-Cys-Xaa₃-Xaa₂-Thr-Xaa₄-Cys-Ser-Xaa₃-Xaa₂ (SEO ID NO:157);

Cys-Cys-Ser-Asn-Xaa₃-Thr-Cys-Xaa₃-Xaa₁-Thr-Xaa₄-Gly-Cys (SEQ ID NO:158);
Cys-Cys-Ala-Asn-Xaa₃-Ile-Cys-Xaa₂-Asn-Thr-Xaa₃-Gly-Cys (SEQ ID NO:159);
Cys-Cys-Asn-Asn-Xaa₃-Thr-Cys-Xaa₂-Xaa₁-Thr-Xaa₄-Gly-Cys (SEQ ID NO:160);
Cys-Cys-Ser-Asn-Xaa₃-Val-Cys-Xaa₂-Xaa₁-Thr-Xaa₄-Gly-Cys (SEQ ID NO:161);

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Gly-Gly-Cys-Cys-Ser-Xaa₄-Xaa₅-Xaa₅-Cys-Ile-Ala-Ser-Asn-Xaa₅-Xaa₂-Cys-Gly (SEQ ID NO:162);

Gly-Cys-Cys-Ser-His-Xaa₃-Val-Cys-Ser-Ala-Met-Ser-Xaa₃-Ile-Cys (SEQ ID NO:163);

Gly-Cys-Cys-Xaa₂-Asn-Xaa₃-Xaa₄-Cys-Gly-Ala-Ser-Xaa₂-Thr-Xaa₄-Cys (SEQ ID NO:164):

Gly-Cys-Cys-Ser-Xaa₄-Xaa₅-Xaa₅-Cys-Phe-Ala-Thr-Asn-Xaa₅-Asp-Cys (SEQ ID NO:165):

Gly-Gly-Cys-Cys-Ser-Xaa₄-Xaa₅-Xaa₅-Cys-Ile-Ala-Asn-Asn-Xaa₅-Leu-Cys-Ala (SEO ID NO:166);

Gly-Gly-Cys-Cys-Ser-Xaa₄-Xaa₅-Xaa₅-Cys-Ile-Ala-Asn-Asn-Xaa₅-Phe-Cys-Ala (SEQ ID NO:167);

Asp-Cys-Ser-Asn-Xaa₃-Xaa₃-Cys-Ser-Gln-Asn-Asn-Xaa₃-Asp-Cys-Met (SEQ ID NO:168); and

Asp-Cys-Cys-Ser-Asn-Xaa₃-Xaa₃-Cys-Ala-His-Asn-Asn-Xaa₃-Asp-Cys-Arg (SEQ ID NO:169),

wherein Xaa_1 is Glu or γ -carboxy-Glu (Gla); Xaa_2 is Lys, N-methyl-Lys, N, N-dimethyl-Lys or N, N, N-trimethyl-Lys; Xaa_3 is Trp (D or L), halo-Trp or neo-Trp; Xaa_4 is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa_3 is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

- 12. The substantially pure α-conotoxin peptide of claim 11, wherein Xaa₂ is Lys.
- 13. The substantially pure α -conotoxin peptide of claim 11, wherein Xaa $_1$ is Glu.
- 14. The substantially pure α-conotoxin peptide of claim 11, wherein Xaa₃ is Trp.
- 15. The substantially pure α -conotoxin peptide of claim 11, wherein Xaa₄ is Tyr.
- The substantially pure α-conotoxin peptide of claim 11, wherein Xaa₄ is mono-iodo-Tyr.
 - 17. The substantially pure α-conotoxin peptide of claim 11, wherein Xaa₄ is di-iodo-Tyr.

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- The substantially pure α-conotoxin peptide of claim 10, which is modified to contain an O-glycan, an S-glycan or an N-glycan.
- The substantially pure α-conotoxin peptide of claim 11 which is modified to contain an O-glycan, an S-glycan or an N-glycan.

A substantially pure α-conotoxin peptide having the generic formula III: Xaa₁-Xaa₂-Xaa₃-Xaa,-Xaa,-Cys-Cys-Xaa,-Xaa,-Xaa,-Xaa,-Cys-Xaa,0-Xaa,1-Cys-Xaa₁₇-Xaa₁₈-Xaa₁₉-Xaa₂₀-Xaa₂₁-Xaa₂₂-Xaa₂₃-Xaa₂₄ (SEQ ID NO:3), wherein Xaa, is des-Xaa₁, Ser or Thr; Xaa₂ is des-Xaa₂, Asp, Glu, γ-carboxy-Glu (Gla), Asn, Ser or Thr; Xaa₃ is des-Xaa3, Ala, Gly, Asn, Ser, Thr, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa, is des-Xaa, Ala, Val, Leu, Ile, Gly, Glu, Gla, Gln, Asp, Asn, Phe, Pro, hydroxy-Pro or any unnatural aromatic amino acid; Xaa5 is des-Xaa5, Thr, Ser, Asp, Glu, Gla, Gln, Gly, Val, Asp, Asn, Ala, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa, is Thr, Ser, Asp, Asn, Met, Val, Ala, Gly, Leu, Ile, Phe, any unnatural aromatic amino acid, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tvr or any unnatural hydroxy containing amino acid; Xaa, is Ile, Leu, Val, Ser, Thr, Gln, Asn, Asp, Arg, His, halo-His, Phe, any unnatural aromatic amino acid, homoarginine, ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaaa is Pro, hyroxy-Pro, Ser, Thr, Ile, Asp. Leu, Val, Gly, Ala, Phe, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaao is Val, Ala, Gly, Ile, Leu, Asp, Ser, Thr, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa10 is His, halo-His, Arg, homoarginine, ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Asn, Ala, Ser, Thr, Phe, Ile, Leu, Gly, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa₁₁ is Leu, Gln, Val, Ile,

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Glv, Met, Ala, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, Ser, Thr, Arg, homoarginine, ornithine, any unnatural basic amino acid, Asn, Glu, Gla, Gln, Phe, Trp (D or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid; Xaa12 is Glu, Gla, Gln, Asn, Asp, Pro, hydroxy-Pro, Ser, Gly, Thr, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,Ntrimethyl-Lys, Arg, homoarginine, ornithine, any unnatural basic amino acid, Phe, His, halo-His, any unnatural aromatic amino acid, Leu, Met, Gly, Ala, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa; is His, halo-His, Asn, Thr, Ser, Ile, Val, Leu, Phe, any unnatural aromatic amino acid, Arg, homoarginine, ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,Ntrimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Try, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa₁₄ is Ser, Thr, Ala, Gln, Pro, hydroxy-Pro, Gly, Ile, Leu, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid: Xaa, is Asn. Glu, Gla, Asp, Gly, His, halo-His, Ala, Leu, Gln, Arg, ornithine, homoarginine, Lvs, N-methyl-Lvs, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa16 is Met, Ile, Thr, Ser, Val, Leu, Pro, hydroxy-Pro, Phe, any unnatural aromatic amino acid, Tyr, nor-Tyr, mono-halo-Tvr. di-halo-Tvr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, any unnatural hydroxy containing amino acid, Glu, Gla, Ala, His, halo-His, Arg, ornithine, homoarginine, Lys, Nmethyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa₁₇ is des-Xaa₁₇, Gly, Asp, Asn, Ala, Ile, Leu, Ser, Thr, His, halo-His, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa18 is des-Xaa18, Gly, Glu, Gla, Gln, Trp (D or L), neo, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa19 is des-Xaa₁₉, Ser, Thr, Val, Ile, Ala, Arg, omithine, homoarginine, Lys, N-methyl-Lys, N,Ndimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa20 is des-Xaa20, Val, Asp, His, halo-His, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa21 is des-Xaa21, Asn, Pro or hydroxy-Pro; Xaa22 is des-Xaa22, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,Ndimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid; Xaa23 is des-Xaa23,

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Ser or Thr; Xaa_{24} is des- Xaa_{24} , Leu, Ile or Val; and the C-terminus contains a free carboxyl group or an amide group, with the proviso that (a) Xaa_5 is not Gly, when Xaa_1 is des- Xaa_4 , Xaa_2 is des- Xaa_2 , Xaa_3 is des- Xaa_3 , Xaa_4 is des- Xaa_4 , Xaa_6 is Ser, Xaa_7 is His, Xaa_8 is Pro, Xaa_9 is Ala, Xaa_{10} is Ser, Xaa_{11} is Val, Xaa_{12} is Asn, Xaa_{13} is Asn, Xaa_{14} is Pro, Xaa_{15} is Asp, Xaa_{16} is Ile, Xaa_{17} is des- Xaa_{17} , Xaa_{18} is des- Xaa_{18} , Xaa_{19} is des- Xaa_{19} , Xaa_{20} is des- Xaa_{20} , Xaa_{21} is des- Xaa_{21} , Xaa_{22} is des- Xaa_{22} , Xaa_{23} is des- Xaa_{23} , and Xaa_{24} is des- Xaa_{24} .

 A substantially pure α-conotoxin peptide of generic forumula III selected from the group consisting of:

Gly-Cys-Cys-Ser-Asn-Xaa₃-Val-Cys-His-Leu-Xaa₁-His-Ser-Asn-Met-Cys (SEQ ID NO:22);

Gly-Cys-Cys-Ser-Asn-Xaa₅-Val-Cys-Arg-Gln-Asn-Asn-Ala-Xaa₁-Xaa₄-Cys-Arg (SEQ ID NO:23);

Xaa,-Gln-Cys-Cys-Ser-His-Xaa,-Ala-Cys-Asn-Val-Asp-His-Xaa,-Xaa,-Ile-Cys-Arg (SEQ ID NO:24);

 $Xaa_5\text{-}Xaa_1\text{-}Cys\text{-}Cys\text{-}Ser\text{-}His\text{-}Xaa_5\text{-}Ala\text{-}Cys\text{-}Asn\text{-}Val\text{-}Asp\text{-}His\text{-}Xaa_5\text{-}Xaa_1\text{-}Ile\text{-}Cys\text{-}Arg} \\ (SEQ ID NO:25);$

 $Xaa_{5}\text{-}Gln\text{-}Cys\text{-}Cys\text{-}Ser\text{-}His\text{-}Xaa_{5}\text{-}Ala\text{-}Cys\text{-}Asn\text{-}Val\text{-}Asp\text{-}His\text{-}Xaa_{5}\text{-}Xaa_{1}\text{-}Ile\text{-}Cys\text{-}Asp}$ (SEQ ID NO:26);

Xaa₅-Arg-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Ile-Cys-Arg (SEQ ID NO:27);

Xaa₅-Gln-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Gly-Ile-Cys-Arg (SEO ID NO:28);

Xaa₅-Gln-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Thr-Cys-Arg (SEO ID NO:29);

Xaa₅-Gln-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Val-Cys-Arg (SEO ID NO:30);

 $Xaa_5\text{-}Gln\text{-}Cys\text{-}Cys\text{-}Ser\text{-}His\text{-}Xaa_5\text{-}Ala\text{-}Cys\text{-}Asn\text{-}Ile\text{-}Asp\text{-}His\text{-}Xaa_5\text{-}Xaa_1\text{-}Ile\text{-}Cys\text{-}Arg} \\ (SEQ ID NO:31);$

Xaa₃-Gln-Cys-Cys-Ser-His-Xaa₃-Ala-Cys-Asn-Val-Asp-His-Xaa₃-Xaa₁-Ile-Cys-Arg-Arg-Arg-Arg (SEQ ID NO:32);

Gly-Gly-Cys-Cys-Ser-His-Xaa₃-Ala-Cys-Ala-Val-Asn-His-Xaa₃-Xaa₁-Leu-Cys (SEQ ID NO:33);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Val-Asn-His-Xaa₅-Xaa₁-Leu-Cys (SEQ ID NO:34):

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Ile-Cys (SEQ ID NO:35);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Gly-Xaa₂-Thr-Gln-Xaa₁-Xaa₅-Cys-Arg-Xaa₁-Ser (SEO ID NO:36);

Xaa₅-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Gly-Asn-Asn-Xaa₅-Xaa₁-Phe-Cys-Arg-Gln (SEQ ID NO:37);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Gly-Asn-Asn-Xaa₅-Xaa₁-Phe-Cys-Arg-Gln (SEQ ID NO:38);

Gly-Cys-Cys-Ser-His-Xaa₃-Xaa₅-Cys-Ala-Met-Asn-Asn-Xaa₃-Asp-Xaa₄-Cys (SEQ ID NO:39);

Gly-Cys-Cys-Ser-His-Xaa₅-Xaa₅-Cys-Phe-Leu-Asn-Asn-Xaa₅-Asp-Xaa₄-Cys (SEQ ID NO:40):

Gly-Cys-Cys-Ser-Asn-Xaa₅-Xaa₅-Cys-Ile-Ala-Xaa₂-Asn-Xaa₅-His-Met-Cys-Gly (SEQ ID NO:41);

Gly-Cys-Cys-Ser-Asn-Xaa₅-Ala-Cys-Ala-Gly-Asn-Asn-Xaa₅-His-Val-Cys-Arg-Gln (SEO ID NO:43):

Gly-Cys-Cys-Ser-Arg-Xaa₃-Ala-Cys-Ile-Ala-Asn-Asn-Xaa₃-Asp-Leu-Cys (SEQ ID NO:44):

 $Gly-Cys-Cys-Ser-Asn-Xaa_5-Val-Cys-His-Val-Xaa_1-His-Xaa_5-Xaa_1-Leu-Cys-Arg-Arg-Arg-Arg-QSEQ ID NO:45); \\$

 $Gly-Gly-Cys-Cys-Ser-Phe-Xaa_5-Ala-Cys-Arg-Xaa_2-Xaa_5-Arg-Xaa_5-Xaa_1-Met-Cys-Gly \ (SEQ\ ID\ NO:46);$

 $Xaa_5\text{-}Xaa_1\text{-}Cys\text{-}Cys\text{-}Ser\text{-}Asp\text{-}Xaa_5\text{-}Arg\text{-}Cys\text{-}Asn\text{-}Ser\text{-}Ser\text{-}His\text{-}Xaa_5\text{-}Xaa_1\text{-}Leu\text{-}Cys\text{-}Gly (SEQ ID NO:47);}$

 $Xaa_{3}\text{-}Gln\text{-}Cys\text{-}Cys\text{-}Asp\text{-}Xaa_{3}\text{-}Arg\text{-}Cys\text{-}Asn\text{-}Val\text{-}Gly\text{-}His\text{-}Xaa_{3}\text{-}Xaa_{1}\text{-}Leu\text{-}Cys\text{-}Gly\text{-}(SEQ\text{-}ID\text{-}NO:48);}$

 $Xaa_{5}\text{-}Val\text{-}Cys\text{-}Cys\text{-}Ser\text{-}Asp\text{-}Xaa_{5}\text{-}Arg\text{-}Cys\text{-}Asn\text{-}Val\text{-}Gly\text{-}His\text{-}Xaa_{5}\text{-}Xaa_{1}\text{-}Ile\text{-}Cys\text{-}Gly}$ (SEQ ID NO:49);

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Gly-Cys-Cys-Ser-Arg-Xaa₅-Xaa₅-Cys-lle-Ala-Asn-Asn-Xaa₅-Asp-Leu-Cys (SEQ ID NO:50);

Xaa₅-Gln-Cys-Cys-Ser-His-Leu-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Ile-Cys-Arg (SEO ID NO:51);

Gly-Cys-Cys-Ser-Xaa₄-Phe-Asp-Cys-Arg-Met-Met-Phe-Xaa₅-Xaa₁-Met-Cys-Gly-Xaa₅-Arg (SEO ID NO:52);

Gly-Gly-Cys-Cys-Ser-Phe-Ala-Ala-Cys-Arg-Xaa₂-Xaa₄-Arg-Xaa₅-Xaa₁-Met-Cys-Gly (SEO ID NO:53);

Gly-Gly-Cys-Cys-Phe-His-Xaa₃-Val-Cys-Xaa₄-Ile-Asn-Leu-Leu-Xaa₁-Met-Cys-Arg-Gln-Arg (SEQ ID NO:54);

 $Ser-Ala-Thr-Cys-Cys-Asn-Xaa_4-Xaa_5-Cys-Xaa_4-Xaa_4-Thr-Xaa_4-Xaa_5-Xaa_1-Ser-Cys-Leu (SEQ ID NO:55);$

Ala-Cys-Cys-Ala-Xaa₄-Xaa₅-Cys-Phe-Xaa₁-Ala-Xaa₄-Xaa₅-Xaa₇-Arg-Cys-Leu (SEQ ID NO:56);

 $Asn-Ala-Xaa_1-Cys-Cys-Xaa_4-Xaa_4-Xaa_5-Xaa_5-Cys-Xaa_1-Ala-Xaa_1-Ala-Xaa_4-Xaa_5-Xaa_1-Ile-Cys-Leu (SEQ ID NO:57);$

Xaa₁-Cys-Cys-Thr-Asn-Xaa₅-Val-Cys-His-Ala-Xaa₁-His-Gln-Xaa₁-Leu-Cys-Ala-Arg-Arg (SEQ ID NO:170);

Gly-Cys-Cys-Ser-Asn-Xaa₅-Val-Cys-His-Leu-Xaa₁-His-Ser-Asn-Leu-Cys (SEQ ID NO:171);

 $Xaa_1\text{-}Cys\text{-}Cys\text{-}Thr\text{-}Asn\text{-}Xaa_5\text{-}Val\text{-}Cys\text{-}His\text{-}Val\text{-}Xaa_1\text{-}His\text{-}Gln\text{-}Xaa_1\text{-}Leu\text{-}Cys\text{-}Ala-} \\ Arg\text{-}Arg\text{-}Arg\text{-}(SEQ\text{ ID NO:172});$

Xaa₀-Xaa₁-Cys-Cys-Ser-Xaa₄-Xaa₅-Ala-Cys-Asn-Leu-Asp-His-Xaa₅-Xaa₁-Leu-Cys (SEQ ID NO:173);

 $Xaa_{3}\text{-}Xaa_{1}\text{-}Cys\text{-}Ser\text{-}Asp\text{-}Xaa_{2}\text{-}Arg\text{-}Cys\text{-}Asn\text{-}Ser\text{-}Thr\text{-}His\text{-}Xaa_{3}\text{-}Xaa_{1}\text{-}Leu\text{-}Cys\text{-}Gly (SEQ ID NO:174);}$

Leu-Asn-Cys-Cys-Met-Ile-Xaa₃-Xaa₅-Cys-Xaa₃-Xaa₂-Xaa₂-Xaa₄-Gly-Asp-Arg-Cys-Ser-Xaa₁-Val-Arg (SEQ ID NO:175);

Ala-Phe-Gly-Cys-Cys-Asp-Leu-Ile-Xaa₁-Cys-Leu-Xaa₁-Arg-Xaa₄-Gly-Asn-Arg-Cys-Asn-Xaa₁-Val-His (SEQ ID NO:176);

Leu-Gly-Cys-Cys-Asn-Val-Thr-Xaa₅-Cys-Xaa₃-Xaa₁-Xaa₂-Xaa₄-Gly-Asp-Xaa₂-Cys-Asn-Xaa₁-Val-Arg (SEQ ID NO:177);

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(SEO ID NO:180);

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Asp-Xaa,-Cvs-Cvs-Ser-Asn-Xaa,-Ala-Cvs-Arg-Val-Asn-Asn-Xaa,-His-Val-Cys-Arg-Arg-Arg (SEO ID NO:178); Leu-Asn-Cys-Cys-Ser-Ile-Xaa₅-Gly-Cys-Xaa₃-Asn-Xaa₁-Xaa₄-Xaa₂-Asp-Arg-Cys-

Ser-Xaa₂-Val-Arg (SEO ID NO:179); Gly-Gly-Cys-Cys-Ser-His-Xaa₅-Val-Cys-Xaa₄-Phe-Asn-Asn-Xaa₅-Gln-Met-Cys-Arg

Gly-Gly-Cys-Cys-Ser-His-Xaa₅-Val-Cys-Asn-Leu-Asn-Asn-Xaa₅-Gln-Met-Cys-Arg (SEO ID NO:181);

Gly-Cys-Cys-Ser-His-Xaa₅-Xaa₅-Cys-Xaa₄-Ala-Asn-Asn-Gln-Ala-Xaa₄-Cys-Asn (SEO ID NO:182);

Gly-Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Val-Thr-His-Xaa₅-Xaa₁-Leu-Cys(SEQ ID NO:183);

Gly-Gly-Cys-Cys-Ser-Xaa4-Xaa5-Ala-Cys-Ser-Val-Xaa1-His-Gln-Asp-Leu-Cys-Asp (SEO ID NO:184);

Val-Ser-Cys-Cys-Val-Val-Arg-Xaa5-Cys-Xaa5-Ile-Arg-Xaa4-Gln-Xaa1-Xaa1-Cys-Leu-Xaa1-Ala-Asp-Xaa5-Arg-Thr-Leu (SEQ ID NO:185);

Xaa,-Asn-Cvs-Cvs-Ser-Ile-Xaa,-Gly-Cvs-Xaa,-Xaa,-Xaa,-Xaa,-Gly-Asp-Xaa,-Cys-Ser-Xaa,-Val-Arg (SEQ ID NO:186);

Gly-Cys-Cys-Ser-Asn-Xaas-Val-Cys-His-Leu-Xaa1-His-Xaa5-Asn-Ala-Cys (SEQ ID NO:187);

Gly-Cys-Cys-Ser-Asn-Xaa₅-Ile-Cys-Xaa₄-Phe-Asn-Asn-Xaa₅-Arg-Ile-Cys-Arg(SEQ ID NO:188):

Xaa₁-Cys-Cys-Ser-Gln-Xaa₅-Xaa₅-Cys-Arg-Xaa₂-Xaa₂-His-Xaa₅-Xaa₁-Leu-Cys-Ser (SEO ID NO:189);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ala-Gly-Asn-Asn-Gln-His-Ile-Cys (SEQ ID NO:190):

Gly-Cys-Cys-Ala-Val-Xaa5-Ser-Cys-Arg-Leu-Arg-Asn-Xaa5-Asp-Leu-Cys-Gly-Gly (SEO ID NO:191);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asn-Asn-Xaa₅-His-Ile-Cys (SEQ ID NO:192);

Thr-Xaas-Xaas-Xaas-Xaas-Asn-Xaas-Xaas-Cys-Phe-Ala-Thr-Asn-Ser-Asp-Ile-Cys-Gly (SEQ ID NO:193);

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Asp-Ala-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Ser-Gly-Xaa₂-His-Gln-Asp-Leu-Cys(SEQ ID NO:194):

Xaa₁-Asp-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Leu-Cys(SEQ ID NO:195):

Gly-Cys-Cys-Ser-His-Xaas-Ala-Cys-Ala-Gly-Ser-Asn-Ala-His-Ile-Cys (SEQ ID NO:196);

Xaa₁-Asp-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Met-Cys (SEQ ID NO:197);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ala-Gly-Asn-Asn-Xaa₅-His-Ile-Cys (SEQ ID NO:198);

Gly-Cys-Cys-Gly-Asn-Xaa₅-Ser-Cys-Ser-Ile-His-Ile-Xaa₅-Xaa₄-Val-Cys-Asn (SEQ ID NO:199);

Thr-Asp-Ser-Xaa_i-Xaa_i-Cys-Cys-Leu-Asp-Ser-Arg-Cys-Ala-Gly-Gln-His-Gln-Asp-Leu-Cys-Gly (SEQ ID NO:200);

Gly-Cys-Cys-Ser-Asn-Xaa₄-Xaa₄-Cys-Xaa₄-Ala-Asn-Asn-Gln-Ala-Xaa₄-Cys-Asn (SEQ ID NO:201);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ser-Val-Asn-Asn-Xaa₅-Asp-Ile-Cys (SEQ ID NO:202);

Gly-Xaa₂-Cys-Cys-Ile-Asn-Asp-Ala-Cys-Arg-Ser-Xaa₂-His-Xaa₅-Gln-Xaa₄-Cys-Ser (SEQ ID NO:203);

 $Gly-Cys-Cys-Xaa_4-Asn-Ile-Ala-Cys-Arg-Ile-Asn-Asn-Xaa_5-Arg-Xaa_4-Cys-Arg(SEQ)$ ID NO:204):

 $Gly\text{-}Cys\text{-}Cys\text{-}Ser\text{-}His\text{-}Xaa_5\text{-}Val\text{-}Cys\text{-}Arg\text{-}Phe\text{-}Asn\text{-}Xaa_4\text{-}Xaa_5\text{-}Xaa_2\text{-}Xaa_4\text{-}Cys\text{-}Gly$ (SEO ID NO:205):

Asp-Xaa₁-Cys-Cys-Ala-Ser-Xaa₅-Xaa₅-Cys-Arg-Leu-Asn-Asn-Xaa₅-Xaa₄-Val-Cys-His (SEQ ID NO:206);

Xaa₁-Ser (SEQ ID NO:207);

 $Gly\text{-}Cys\text{-}Cys\text{-}Ser\text{-}His\text{-}Xaa_s\text{-}Xaa_s\text{-}Cys\text{-}Ala\text{-}Gln\text{-}Asn\text{-}Asn\text{-}Gln\text{-}Asp\text{-}Xaa_d\text{-}Cys} \\ (SEQ)$ ID NO:208);

Gly-Cys-Cys-Ser-His-Xaa₄-Ala-Cys-Ser-Gly-Asn-Asn-Arg-Xaa₄-Cys-Arg-Xaa₁-Ser (SEQ ID NO:209);

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Asp-Xaa₃-Cys-Cys-Ser-Xaa₄-Xaa₃-Asp-Cys-Gly-Ala-Asn-His-Xaa₃-Xaa₁-Ile-Cys-Gly (SEQ ID NO:210);

Xaa₁-Cys-Cys-Ser-Gln-Xaa₅-Xaa₅-Cys-Arg-Xaa₂-His-Xaa₅-Xaa₁-Leu-Cys-Ser (SEO ID NO:211);

Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Ala-Gly-Asn-Asn-Xaa₅-His-Ile-Cys (SEQ ID NO:212):

Gly-Cys-Cys-Ser-Asp-Xaa₃-Ser-Cys-Asn-Val-Asn-Asn-Xaa₃-Asp-Xaa₄-Cys (SEQ ID NO:213):

Xaa₁-Xaa₁-Cys-Cys-Ser-Asp-Xaa₃-Arg-Cys-Ser-Val-Gly-His-Gln-Asp-Met-Cys-Arg (SEQ ID NO:214);

 $\label{eq:Gly-Gly-Cys-Cys-Ser-Asn-Xaa} Gly-Gly-Cys-Cys-Ser-Asn-Xaa_3-Ala-Cys-Leu-Val-Asn-His-Leu-Xaa_1-Met-Cys (SEQ ID NO:215);$

Arg-Asp-Xaa₅-Cys-Cys-Phe-Asn-Xaa₅-Ala-Cys-Asn-Val-Asn-Asn-Xaa₅-Gln-Ile-Cys (SEQ ID NO:216);

Cys-Cys-Ser-Asp-Xaa₃-Ser-Cys-Xaa₃-Arg-Leu-His-Ser-Leu-Ala-Cys-Thr-Gly-Ile-Val-Asn-Arg (SEQ ID NO:217);

Cys-Cys-Thr-Asn-Xaa₅-Ala-Cys-Leu-Val-Asn-Asn-Ile-Arg-Phe-Cys-Gly (SEQ ID NO:218);

Asp-Xaa₁-Cys-Cys-Ser-Asp-Xaa₅-Arg-Cys-His-Gly-Asn-Asn-Arg-Asp-His-Cys-Ala (SEO ID NO:219);

 $\label{eq:asp-Cys-Ser-His-Xaa} Asp-Cys-Ser-His-Xaa_5-Leu-Cys-Arg-Leu-Phe-Val-Xaa_5-Gly-Leu-Cys-Ile(SEQ\ ID\ NO:220);$

Gly-Cys-Cys-Ser-His-Xaa₅-Val-Cys-Xaa₂-Val-Arg-Xaa₄-Xaa₅-Asp-Leu-Cys-Arg (SEQ ID NO:221);

Gly-Cys-Cys-Ser-His-Xaa₃-Ala-Cys-Asn-Val-Asn-Asn-Xaa₃-His-Ile-Cys (SEQ ID NO:222):

Gly-Cys-Cys-Ser-His-Xaa₃-Val-Cys-Xaa₂-Val-Arg-Xaa₄-Ser-Asp-Met-Cys(SEQID NO:223):

Gly-Gly-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Xaa₂-Val-His-Phe-Xaa₅-His-Ser-Cys(SEQ ID NO:224):

Val-Cys-Cys-Ser-Asn-Xaa₅-Val-Cys-His-Val-Asp-His-Xaa₅-Xaa₁-Leu-Cys-Arg-Arg-Arg-Arg (SEQ ID NO:225);

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Gly-Cys-Ser-His-Xaa₃-Val-Cys-Asn-Leu-Ser-Asn-Xaa₃-Gln-lle-Cys-Arg (SEQ ID NO:226):

Xaa₅-Xaa₁-Cys-Cys-Ser-His-Xaa₅-Ala-Cys-Asn-Val-Asp-His-Xaa₅-Xaa₁-Ile-Cys-Arg (SEQ ID NO:227);

Gly-Cys-Cys-Ser-Asn-Xaa₃-Ala-Cys-Leu-Val-Asn-His-Ile-Arg-Phe-Cys-Gly (SEQ ID NO:228);

Asp-Cys-Cys-Asp-Asp-Xaa₅-Ala-Cys-Thr-Val-Asn-Asn-Xaa₅-Gly-Leu-Cys-Thr (SEQ ID NO:229); and

Gly-Cys-Cys-Ser-Asn-Xaa $_5$ -Xaa $_5$ -Cys-Ile-Ala-Xaa $_2$ -Asn-Xaa $_5$ -His-Met-Cys-Gly-Gly-Arg-Arg (SEQ ID NO:230), wherein Xaa $_1$ is Glu or γ -carboxy-Glu (Gla); Xaa $_2$ is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa $_3$ is Trp (D or L), halo-Trp or neo-Trp; Xaa $_4$ is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa $_4$ is Pro or hydroxy-Pro; Xaa $_4$ is Gln or pyro-Glu; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

- The substantially pure α-conotoxin peptide of claim 21, wherein Xaa₂ is Lys.
- The substantially pure α-conotoxin peptide of claim 21, wherein Xaa₁ is Glu.
- 24. The substantially pure α -conotoxin peptide of claim 21, wherein Xaa $_3$ is Trp.
- The substantially pure α-conotoxin peptide of claim 21, wherein Xaa₄ is Tyr.
- 26. The substantially pure α -conotoxin peptide of claim 21, wherein Xaa₄ is mono-iodo-Tyr.
- 27. The substantially pure α -conotoxin peptide of claim 21, wherein Xaa₄ is di-iodo-Tyr.
- The substantially pure α-conotoxin peptide of claim 20, which is modified to contain an Oglycan, an S-glycan or an N-glycan.

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- 29 The substantially pure α-conotoxin peptide of claim 21 which is modified to contain an O-glycan, an S-glycan or an N-glycan.
- 30. A substantially pure α -conotoxin peptide selected from the group consisting of:

 $\label{eq:cys-Cys-Xaa_2-Xaa_2-Xaa_2-Xaa_2-Xaa_2-Xaa_2-Xaa_2-Ala-Cys-Val-Phe (SEQ ID NO:231) and} Cys-Val-Phe (SEQ ID NO:231) and$

Gly-Cys-Cys-Gly-Asn-Xaa₃-Ala-Cys-Ser-Gly-Ser-Ser-Xaa₂-Asp-Ala-Xaa₃-Ser-Cys (SEQ ID NO:232), wherein Xaa₁ is Glu or γ-carboxy-Glu (Gla); Xaa₂ is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N,N,N-trimethyl-Lys; Xaa₁ is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; and Xaa₃ is Pro or hydroxy-Pro; and the C-terminus contains a carboxyl or amide group, or derivatives thereof.

- 31. The substantially pure α -conotoxin peptide of claim 30, wherein Xaa_2 is Lys.
- 32. The substantially pure α -conotoxin peptide of claim 30, wherein Xaa $_1$ is Glu.
- 33. The substantially pure α -conotoxin peptide of claim 30, wherein Xaa $_4$ is Tyr.
- 15 34. The substantially pure α-conotoxin peptide of claim 30, wherein Xaa₄ is mono-iodo-Tyr.
 - 35. The substantially pure α-conotoxin peptide of claim 30, wherein Xaa₄ is di-iodo-Tyr.
 - 36. The substantially pure α-conotoxin peptide of claim 30, which is modified to contain an O-glycan, an S-glycan or an N-glycan.
 - 37. An isolated nucleic acid comprising a nucleic acid coding for an α -conotoxin precursor comprising an amino acid sequence selected from the group of amino acid sequences set forth in Tables 1-134.

- 38. The nucleic acid of claim 37 wherein the nucleic acid comprises a nucleotide sequence selected from the group of nucleotide sequences set forth in Tables 1-134 or their complements.
- A substantially pure α-conotoxin protein precursor comprising an amino acid sequence selected from the group of amino acid sequences set forth in Tables 1-134.

TITLE OF THE INVENTION ALPHA-CONOTOXIN PEPTIDES

ABSTRACT OF THE DISCLOSURE

The invention relates to relatively short peptides (termed α -conotoxins herein), about 10-30 residues in length, which are naturally available in minute amounts in the venom of the cone snails or analogous to the naturally available peptides, and which preferably include two disulfide bonds.

SEQUENCE LISTING

```
<110> Watkins, Maren
      Olivera, Baldomero M.
      Hillyard, David R.
      McIntosh, J. Michael
      Jones, Robert M.
<120> Alpha-Conotoxin Peptides
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<130> Alphas 2
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<150> US 60/118,381

<151> 1999-01-29

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<170> PatentIn Ver. 2.0

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<212> PRT

<213> Artificial Seguence

<220>

<223> Description of Artificial Sequence: Alpha-Conotoxin Peptide Generic Formula I

<220>

<221> PEPTIDE

<223> Xaa at residue 1 is des-Xaa, Ile, Leu or Val; Xaa at residue 2 is des-Xaa, Ala or Gly; Xaa at residue 3 is des-Xaa, Gly, Trp (D or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid.

<221> PEPTIDE

<222> (4)..(5)

<223> Xaa at residue 4 is des-Xaa, Gly, Trp (D or L), neo-Trp, halo-Trp or any unnatural aromatic amino acid; Xaa at residue 5 is Glu, gamma-carboxy-Glu (Gla), Asp, Ala, Thr, Ser, Gly, Ile, Tyr, nor-Tyr,

<220>

<221> PEPTIDE

<222> (5)..(8)

<223> mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa at residue 8 is Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys,

<220>

<221> PEPTIDE

<222> (8)..(9)

<223> N.N-dimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid; Xaa at residue 9 is Asp, Glu, Gla, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or

<220> <221> PEPTIDE <222> (9)..(11) <223> any unnatural basic amino acid; Xaa at residue 10 is Ser, Thr, Asn, Ala, Gly, His, halo-His, Pro or hydroxy-Pro; Xaa at residue 11 is Thr, Ser, Ala, Asp, Asn, Pro, hydroxy-Pro, <220> <221> PEPTIDE <223> Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or any unnatural basic amino acid: Xaa at residue 13 is Gly, Ser, Thr, Ala, Asn, <221> PEPTIDE <222> (13)..(14) <223> Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or any unnatural basic amino acid; Xaa at residue 14 Gln, Leu, His, halo-His, Trp (D or L), halo-Trp, neo-Tro. <220> <221> PEPTIDE <222> (14) <223> Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys, any unnatural basic amino <220> <221> PEPTIDE <222> (14)..(15) <223> acid or any unnatural aromatic amino acid; Xaa at residue 15 is Asn, His, halo-His, Ile, Leu, Val, Gln, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or any <220> <221> PEPTIDE <222> (15)..(16) <223> unnatural basic amino acid; Xaa at residue 16 is des-Xaa, Val, Ile, Leu, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N, N, N-trimethyl-Lys or any unnatural basic amino acid.

Xaa Xaa Xaa Xaa Xaa Cys Cys Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Cys

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<210> 2 <211> 21 <212> PRT <213> Artificial Sequence <220>
<223> Description of Artificial Sequence:Alpha-Conotoxin
Peptide Generic Formula II.

<220> <221> PEPTIDE

<222> (1)..(3)
<223> Xaa at residue 1 is des-Xaa, Asp, Glu or
gamma-carboxy-Glu (Gla); Xaa at residue 2 is
des-Xaa, Gln, Ala, Asp, Glu, Gla; Xaa at residue 3
is des-Xaa, Gly, Ala, Asp, Glu, Gla, Pro or
hydroxy-Pro.

<220> <221> PEPTIDE

<222> (4)..(7)
<223> Xaa at residue 4 is des-Xaa4, Gly, Glu, Gla, Gln,
Asp, Asn, Pro or hydroxy-Pro; Xaa at residue 7 is
Ser, Thr, Gly, Glu, Gla, Asn, Trp (D or L),
neo-Trp, halo-Trp, Arg, ornithine, homoarginine,

<221> PEPTIDE <222> (7)

2233 Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy

<220> <221> PEPTIDE

<222> (7)..(8)

<223> containing amino acid; Xaa at residue 8 is Asp, Asn, His, halo-His, Thr, Ser, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phosoho-Tyr, nitro-Tyr or any unnatural hydroxy

<220> <221> PEPTIDE

<222> (8)..(10)

<223> containing amino acid; Xaa at residue 9 is Pro or hydroxy-Pro; Xaa at residue 10 is Ala, Ser, Thr, Asp, Val, Ile, Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,

<220> <221> PEPTIDE

<222> (10)...(12)
<223> O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy
containing amino acid; Xaa at residue 12 is Gly,
Ile, Leu, Val, Ala, Thr, Ser, Pro, hydroxy-Pro,
Phe, Trp (D or L), neo-Trp, halo-Trp, Arg,

<220>

<221> PEPTIDE

<222> (12)..(13)

ornithine.

<223> homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid or any unnatural aromatic amino acid; Xaa at residue 13 is Ala, Asn, Phe, Pro, hydroxy-Pro,

<220>

<221> PEPTIDE

<222> (13)

<223> Glu, Gla, Gln, His, halo-His, Val, Ser, Thr, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N-trimethyl-Lys or any unnatural basic amino acid.

<220>

<221> PEPTIDE

<222> (14)

<223> Xaa at residue 14 is Thr, Ser, His, halo-His, Leu, Ile, Val, Asn, Met, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys, any unnatural basic

<220>

<221> PEPTIDE

<222> (14) . (15)

<2233 amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa at residue 15 is Asn, Pro, hydroxy-Pro, Gln, Ser, Thr,</p>

<220> <221> PEPTIDE

<222> (15)

<223> Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr

<220> <221> PEPTIDE

<222> (15)..(16)

<223> or any unnatural hydroxy containing amino acid; Xaa at residue 16 is des-Xaa, Gly, Thr, Ser, Pro, hydroxy-Fro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any

2205

<221> PEPTIDE

<222> (16)..(17)

<223> unnatural hydroxy containing amino acid; Xaa at residue 17 is des-Xaa14, Ile, Val, Asp, Leu, Phe, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N-trimethyl-Lys, any unnatural

<220>

<221> PEPTIDE

<222> (17)..(19)

<223> basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa at residue 19 is des-Xaa, Gly, Ala, Met, Ser,

<220>

<221> PEPTIDE

<222> (19)

<223> Thr, Trp (D or L), neo-Trp, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N-timethyl-Lys or any unnatural basic amino acid.

<220> <221> PEPTIDE

<221> PEPTIDE <222> (20)

<223> Xaa'at residue 20 is des-Xaa, Trp (D or L),
neo-Trp, halo-Trp, any unnatural aromatic amino
acid, Arg, ornithine, homoarqinine, Lys,
N-methyl-Tys, N, N-dimethyl-Lys,
N, N, N-trimethyl-Lys or any

<220> <221> PEPTIDE

<222> (20)..(21)

<223> unnatural basic amino acid; Xaa at residue 21 is des-Xaa, Arg, ornithine, homoarginine, Lys, N-methyl-lys, N,N-dimethyl-lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid.

<400> 2 Xaa Xaa Xaa Xaa Cu

Xaa Xaa Xaa Xaa Cys Cys Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa 1 10 15 15

Xaa Cys Xaa Xaa Xaa 20

<210> 3 <211> 28

<212> PRT <213> Artificial Sequence

220>

<223> Description of Artificial Sequence: Alpha-Conotoxin Peptide Generic Formula III.

<220>

<221> PEPTIDE <222> (1)..(3)

<223> Xaa at residue 1 is des-Xaa, Ser or Thr; Xaa at
residue 2 is des-Xaa, Asp, Glu, --carboxy-Glu
(Gla), Asn, Ser or Thr; Xaa at residue 3 is
des-Xaa, Ala, Gly, Asn, Ser, Thr, Pro,
hydroxy-Pro, Arq,

<220>

<221> PEPTIDE <222> (3)..(4)

<223> ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa at residue 4 is des-Xaa, Ala, Val, Leu, Ile, Gly, Glu, Gla, Gln, Asp, Asn, Phe

<220> <221> PEPTIDE

<222> (4)..(5) <223> Pro, hydroxy-Pro or any unnatural aromatic amino acid; Xaa at residue 5 is des-Xaa, Thr, Ser, Asp,

Glu, Gla, Gln, Gly, Val, Asp, Asn, Ala, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys,

<220>

<221> PEPTIDE <222> (5)..(8)

<223> N-methyl-Lys, N, N-dimethyl-Lys,

N, N, N-trimethyl-Lys or any unnatural basic amino acid; Xaa at residue 8 is Thr, Ser, Asp, Asn, Met, Val, Ala, Gly, Leu, Ile, Phe, any unnatural aromatic amino acid,

<220>

<221> PEPTIDE

<222> (8)..(9)

<223> Pro, hydroxy-Pro, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa at residue 9 is Ile, Leu, Val, Ser, Thr, Gln,

<220>

<221> PEPTIDE <222> (9)

<223> Asn, Asp, Arg, His, halo-His, Phe, any unnatural aromatic amino acid, homoarginine, ornithine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Tyr,

<220>

<221> PEPTIDE

<222> (9)..(10)

<223> mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa at residue 10 is Pro, hyroxy-Pro, Ser, Thr, Ile, Asp, Leu, Val, Gly, Ala, Phe,

<220>

<221> PEPTIDE

<222> (10)..(11)

<223> any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or any unnatural basic amino acid; Xaa at residue 11 is Val, Ala, Gly, Ile,

<221> PEPTIDE

<222> (11)..(13)

<223> Leu, Asp, Ser, Thr, Pro, hydroxy-Pro, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or any unnatural basic amino acid; Xaa at residue 13 is His, halo-His,

<221> PEPTIDE

<222> (13)

<223> Arg, homoarginine, ornithine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys, any unnatural basic amino acid, Asn, Ala, Ser, Thr, Phe, Ile, Leu, Gly, Trp (D or L), neo-Trp, halo-Trp, any

<220> <221> PEPTIDE

<221> PEPTID <222> (14)

<223> Gly, Met, Ala, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, Ser, Thr, Arg, homoarginine, ornithine, any unnatural basic amino acid, Asn, Glu, Gla, Gln, Phe, Trp (D or L), neo-Trp,

<220:

<221> PEPTIDE

<222> (14)..(15)

<223> halo-Trp or any unnatural aromatic amino acid; Xaa
at residue 15 is Glu, Gla, Gln, Asn, Asp, Pro,
hydroxy-Pro, Ser, Gly, Thr, Lys, N-methyl-Lys,
N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, Arg,

<220>

<221> PEPTIDE

<222> (15)

<223> homoarginine, ornithine, any unnatural basic amino acid, Phe, His, halo-His, any unnatural aromatic amino acid, Leu, Met, Gly, Ala, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,

<220>

<221> PEPTIDE

<222> (15)..(16)

<223> O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa at residue 16 is His, halo-His, Asn, Thr, Ser, Ile, Val, Leu, Phe, any unnatural aromatic amino acid, Arg, homoarginine,

<220>

<221> PEPTIDE

<222> (16)

<223> ornithine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N,N-trimethyl-Lys, any unnatural basic amino acid, Tyr, nor-Try, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural

220>

<221> PEPTIDE

<222> (16)..(17)

<223> hydroxy containing amino acid; Xaa at residue 17 is Ser, Thr. Ala, Gin, Pro, hydroxy-Pro, Gly, Ile, Leu, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N,N-trimethyl-Lys or any

<220>

<221> PEPTIDE

<222> (17)..(18)

<223> unnatural basic amino acid; Xaa at residue 18 is

Asn, Glu, Gla, Asp, Gly, His, halo-His, Ala, Leu, Gln, Arg, ornithine, homoarginine, Lvs, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys, any

- <220>
- <221> PEPTIDE
- <222> (18)..(19)
- <223> unnatural basic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tyr or any unnatural hydroxy containing amino acid; Xaa at residue 19 is Met, Ile, Thr. Ser,
- <220>
- <221> PEPTIDE
- <222> (19)
- <223> Val, Leu, Pro, hydroxy-Pro, Phe, any unnatural aromatic amino acid, Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr, nitro-Tvr, any unnatural hydroxy containing amino acid,
- <221> PEPTIDE <222> (19)..(21)
- <223> Glu, Gla, Ala, His, halo-His, Arg, ornithine, homoarginine, Lvs, N-methvl-Lvs, N,N-dimethvl-Lvs, N,N,N-trimethyl-Lys or any unnatural basic amino acid; Xaa at residue 21 is des-Xaa, Gly, Asp, Asn,
- <220> <221> PEPTIDE
- <222> (21)..(22)
- <223> Ala, Ile, Leu, Ser, Thr, His, halo-His, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or any unnatural basic amino acid; Xaa at residue 22 is des-Xaa, Glv,
- <220> <221> PEPTIDE
- <222> (22)
- <223> Glu, Gla, Gln, Trp (D or L), neo, halo-Trp, any unnatural aromatic amino acid, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N,N-dimethyl-Lys, N.N.N-trimethyl-Lys or any unnatural basic amino acid.
- <220> <221> PEPTIDE
- <222> (23)
- <223> Xaa at residue 23 is des-Xaa, Ser, Thr, Val, Ile, Ala, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or any unnatural basic amino acid.
- <220>
- <221> PEPTIDE
- <222> (24)
- <223> Xaa at residue 24 is des-Xaa, Val, Asp, His, halo-His, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys,

<400> 6

N, N, N-trimethyl-Lys or any unnatural basic amino acid. <220> <221> PEPTIDE <222> (25)..(26) <223> Xaa at residue 25 is des-Xaa, Asn, Pro or hydroxy-Pro; Xaa at residue 26 is des-Xaa, Arg, ornithine, homoarginine, Lys, N-methyl-Lys, N, N-dimethyl-Lys, N, N, N-trimethyl-Lys or any unnatural basic amino <221> PEPTIDE <222> (26)..(28) <223> acid; Xaa at residue 27 is des-Xaa, Ser or Thr; Xaa at residue 28 is des-Xaa, Leu, Ile or Val. Xaa Xaa Xaa Xaa Xaa Cys Cys Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa Cys Xaa Xaa Xaa Xaa Xaa Xaa Xaa <210> 4 <211> 14 <212> PRT <213> Conus imperialis <220> <221> PEPTIDE <222> (2)..(11) <223> Xaa at residue 2 is Glu or gamma-carboxy-Glu; Xaa at residue 11 is Lys, N-methyl-Lys, N, N-dimethyl-Lys or N, N, N-trimethyl-Lys. <400> 4 Asp Xaa Cys Cys Ser Asp Ser Arg Cys Gly Xaa Asn Cys Leu <210> 5 <211> 12 <212> PRT <213> Conus imperialis <220> <221> PEPTIDE <222> (10) <223> Xaa at residue 10 is Trp (D or L) or halo-Trp. <400> 5 Ala Cys Cys Ser Asp Arg Arg Cys Arg Xaa Arg Cys <210> 6 <211> 13 <212> PRT <213> Conus regius

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10
Phe Thr Cys Cys Arg Arg Gly Thr Cys Ser Gln His Cys
<210> 7
<211> 13
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (2)
<223> Xaa at residue 2 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 7
Asp Xaa Cys Cys Arg Arg His Ala Cys Thr Leu Ile Cys
<210> 8
<211> 13
<212> PRT
<213> Conus regius
<221> PEPTIDE
<222> (2)..(8)
<223> Xaa at residue 2 is Tyr, nor-Tyr, mono-halo-Tyr,
       di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
nitro-Tyr; Xaa at residues 7 and 8 is Pro or
       hydroxy-Pro.
<400> 8
Asp Xaa Cys Cys Arg Arg Xaa Xaa Cys Thr Leu Ile Cys
<210> 9
<211> 13
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (6)..(10)
<223> Xaa at residue 6 is Pro or hdroxy-Pro; Xaa at
       residue 10 is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
       nitro-Tyr.
<400> 9
Gly Cys Cys Ser Asp Xaa Arg Cys Arg Xaa Arg Cys Arg
<210> 10
<211> 13
<212> PRT
<213> Conus regius
<221> PEPTIDE
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<222> (7)..(11)
<223> Xaa at residue 7 is Pro or hydroxy-Pro; Xaa at
     residue 11 is Trp (D or L) or halo-Trp.
<400> 10
Gly Gly Cys Cys Ser Asp Xaa Arg Cys Ala Xaa Arg Cys
<210> 11
<211> 17
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (3)..(10)
<223> Xaa at residue 3 is Trp (D or L) or halo-Trp; Xaa
      at residue 9 is Glu or gamma-carboxy-Glu; Xaa at
      residue 10 is Pro or hydroxy-Pro.
<220>
<221> PEPTIDE
<223> Xaa at residue 15 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 11
Ile Ala Xaa Asp Ile Cys Cys Ser Xaa Xaa Asp Cys Asn His Xaa Cys
                                     10
Val
<210> 12
<211> 12
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (6)..(9)
<223> Xaa at residue 6 is Pro or hydroxy-Pro; Xaa at
      residue 9 is Lys, N-methyl-Lys, N,N-dimethyl-Lys
      or N, N, N-trimethyl-Lys.
<400> 12
Gly Cys Cys Ser Asp Xaa Arg Cys Xaa His Gln Cys
<210> 13
<211> 14
<212> PRT
<213> Conus sponsalis
<221> PEPTIDE
<222> (5)..(11)
<223> Xaa at residues 5 and 11 is Pro or hydroxy-Pro;
      Xaa at residue 8 is Lys, N-methyl-Lys,
      N.N-dimethyl-Lys or N.N.n-trimethyl-Lys.
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<400> 13
Cys Cys Ser Asp Xaa Ala Cys Xaa Gln Thr Xaa Gly Cys Arg
<210> 14
<211> 13
<212> PRT
<213> Conus sponsalis
<220>
<221> PEPTIDE
<222> (3)..(5)
<223> Xaa at residue 3 is Glu or gamma-carboxy-Glu; Xaa
      at residue 5 is Pro or hydroxy-Pro.
Cys Cys Xaa Asn Xaa Ala Cys Arg His Thr Gln Gly Cys
<210> 15
<211> 13
<212> PRT
<213> Conus sulcatus
<220>
<221> PEPTIDE
<222> (4)..(12)
<223> Xaa at residue 4 is Trp or halo-Trp; Xaa at
      residue 6 is Pro or hydroxy-Pro; Xaa at residue 12
      is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr,
      O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr.
<400> 15
Gly Cys Cys Xaa His Xaa Ala Cys Gly Arg His Xaa Cys
<210> 16
<211> 14
<212> PRT
<213> Conus achatinus
<220>
<221> PEPTIDE
<222> (2)..(11)
<223> Xaa at residues 2 and 7 is Pro or hydroxy-Pro; Xaa
      at residue 11 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 16
Ala Xaa Cys Cys Asn Asn Xaa Ala Cys Val Xaa His Arg Cys
<210> 17
<211> 15
<212> PRT
<213> Conus bullatus
<220>
<221> PEPTIDE
<222> (2)..(12)
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13
<223> Xaa at residues 2 and 8 is Pro or hydroxy-Pro; Xaa
      at residue 12 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 17
Ala Xaa Gly Cys Cys Asn Asn Xaa Ala Cys Val Xaa His Arg Cys
<210> 18
<211> 14
<212> PRT
<213> Conus bullatus
<220>
<221> PEPTIDE
<222> (1)..(11)
<223> Xaa at residues 1, 2 and 7 is Pro or hydroxy-Pro;
      Xaa at residue 11 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 18
Xaa Xaa Cys Cys Asn Asn Xaa Ala Cys Val Xaa His Arg Cys
<210> 19
<211> 16
<212> PRT
<213> Conus bullatus
<220>
<221> PEPTIDE
<222> (2)..(13)
<223> Xaa at residue 2 is Glu or gamma-carboxy-Glu; Xaa
      at residue 6 is Trp or halo-Trp; Xaa at residues 8
      11 and 13 is Pro or hydroxy-Pro.
<400> 19
Asp Xaa Asn Cys Cys Xaa Asn Xaa Ser Cys Xaa Arg Xaa Arg Cys Thr
<210> 20
<211> 13
<212> PRT
<213> Conus bullatus
<220>
<221> PEPTIDE
<222> (6)..(12)
<223> Xaa at residues 6 and 7 is Pro or hydroxy-Pro; Xaa
      at residue 12 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 20
Gly Cys Cys Ser Arg Xaa Xaa Cys Ala Val Leu Xaa Cys
<210> 21
<211> 13
<212> PRT
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14
<213> Conus circumcisus
<221> PEPTIDE
<222> (6)
<223> Xaa at residue 6 is Pro or hydroxy-Pro.
<400> 21
Gly Cys Cys Gly Asn Xaa Asp Cys Thr Ser His Ser Cys
<210> 22
<211> 16
<212> PRT
<213> Conus stercusmuscarum
<220>
<221> PEPTIDE
<222> (6)..(11)
<223> Xaa at residue 6 is Pro or hydroxy-Pro; Xaa at
      residue 11 is Glu or gamma-carboxy-Glu.
<400> 22
Gly Cys Cys Ser Asn Xaa Val Cys His Leu Xaa His Ser Asn Met Cys
<210> 23
<211> 17
<212> PRT
<213> Conus obscurus
<220>
<221> PEPTIDE
<222> (6)..(15)
<223> Xaa at residue 6 is Pro or hydroxy-Pro; Xaa at
      residue 14 is Glu or gamma-carboxy-Glu; Xaa at
      residue 15 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 23
Gly Cys Cys Ser Asn Xaa Val Cys Arg Gln Asn Asn Ala Xaa Xaa Cys
                                     10
Arg
<210> 24
<211> 18
<212> PRT
<213> Conus textile
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 24
Xaa Gln Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Ile
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The second secon
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Cys Arg
<210> 25
<211> 18
<212> PRT
<213> Conus radiatus
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
Xaa at residues 2 and 15 is Glu or
      gamma-carboxy-Glu.
<400> 25
Xaa Xaa Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Ile
Cys Arg
<210> 26
<211> 18
<212> PRT
<213> Conus radiatus
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 26
Xaa Gln Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Ile
Cys Asp
<210> 27
<211> 18
<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 27
Xaa Arg Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Ile
Cys Arg
<210> 28
<211> 18
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<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (1)..(14)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro.
<400> 28
Xaa Gln Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Gly Ile
Cys Arg
<210> 29
<211> 18
<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 29
Xaa Gln Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Thr
Cys Arg
<210> 30
<211> 18
<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 30
Xaa Gln Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Val
Cys Arg
<210> 31
<211> 18
<212> PRT
<213> Conus omaria
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
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<211> 16

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<400> 31
Xaa Gln Cys Cys Ser His Xaa Ala Cys Asn Ile Asp His Xaa Xaa Ile
Cys Arg
<210> 32
<211> 21
<212> PRT
<213> Conus omaria
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 32
Xaa Gln Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Ile
Cys Arg Arg Arg Arg
<210> 33
<211> 17
<212> PRT
<213> Conus betulinus
<220>
<221> PEPTIDE
<222> (7)..(15)
<223> Xaa at residues 7 and 14 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 33
Gly Gly Cys Cys Ser His Xaa Ala Cys Ala Val Asn His Xaa Xaa Leu
Cys
<210> 34
<211> 16
<212> PRT
<213> Conus betulinus
<220>
<221> PEPTIDE
<222> (6)..(14)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
      Xaa at residue 14 is Glu or gamma-carboxy-Glu.
<400> 34
Gly Cys Cys Ser His Xaa Ala Cys Ser Val Asn His Xaa Xaa Leu Cys
                                      10
<210> 35
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<212> PRT
<213> Conus dalli
<220>
<221> PEPTIDE
<222> (6)..(14)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
      Xaa at residue 14 is Glu or gamma-carboxy-Glu.
<400> 35
Gly Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Ile Cys
<210> 36
<211> 19
<212> PRT
<213> Conus obscurus
<220>
<221> PEPTIDE
<222> (6)..(18)
<223> Xaa at residues 6 and 15 is Pro or hydroxy-Pro;
      Xaa at reside 11 is Lys, N,-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys; Xaa at
      residues 14 and 18 is Glu or gamma-carboxy-Glu.
<400> 36
Gly Cys Cys Ser His Xaa Ala Cys Ser Gly Xaa Thr Gln Xaa Xaa Cys
                                        10
Arg Xaa Ser
<210> 37
<211> 18
<212> PRT
<213> Conus tulipa
<220>
<221> PEPTIDE
<222> (1)..(14)
<223> Xaa at residues 1, 6 and 13 is Pro or hydroxy-Pro;
Xaa at residue 14 is Glu or gamma-carboxy-Glu.
<400> 37
Xaa Cys Cys Ser His Xaa Ala Cys Ser Gly Asn Asn Xaa Xaa Phe Cys
                                        10
Arg Gln
<210> 38
<211> 18
 <212> PRT
 <213> Conus tulipa
<220>
 <221> PEPTIDE
<222> (6)..(14)
 <223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
       Xaa at residue 14 is Glu or gamma-carboxy-Glu.
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<400> 38
Gly Cys Cys Ser His Xaa Ala Cys Ser Gly Asn Asn Xaa Xaa Phe Cys
Ara Gln
<210> 39
<211> 16
<212> PRT
<213> Conus pennaceus
<221> PEPTIDE
<222> (6)..(15)
<223> Xaa at residues 6, 7 and 13 is Pro or hydroxy-Pro;
Xaa at residue 15 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 39
Gly Cys Cys Ser His Xaa Xaa Cys Ala Met Asn Asn Xaa Asp Xaa Cys
<210> 40
<211> 16
<212> PRT
<213> Conus pennaceus
<220>
<221> PEPTIDE
<222> (6)..(15)
<223> Xaa at residuew 6, 7 and 13 is Pro or hydroxy-Pro;
       Xaa at residue 15 is Tyr, nor-Tyr, mono-halo-Tyr,
       di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
       nitro-Tyr.
 Gly Cys Cys Ser His Xaa Xaa Cys Phe Leu Asn Asn Xaa Asp Xaa Cys
<210> 41
 <211> 17
 <212> PRT
 <213> Conus textile
 <221> PEPTIDE
 <222> (6)..(13)
 <223> Xaa at residues 6, 7 and 13 is Pro or hydroxy-Pro;
       Xaa at residue 11 is Lys, N-methyl-Lys,
       N, N-dimethyl-Lys or N.N.N-trimethyl-Lys.
 <400> 41
 Gly Cys Cys Ser Asn Xaa Xaa Cys Ile Ala Xaa Asn Xaa His Met Cys
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 Gly
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and the state of t
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<210> 42
<211> 16
<212> PRT
<213> Conus distans
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6, 7 and 13 is Pro or hydroxy-Pro.
<400> 42
Gly Cys Cys Ser Asn Xaa Xaa Cys Ala His Asn Asn Xaa Asp Cys Arg
<210> 43
<211> 17
<212> PRT
<213> Conus tulipa
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 43
Gly Cys Cys Ser Asn Xaa Ala Cys Ala Gly Asn Asn Xaa His Val Cys
Arq
<210> 44
<211> 16
<212> PRT
<213> Conus dalli
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 44
Gly Cys Cys Ser Arg Xaa Ala Cys Ile Ala Asn Asn Xaa Asp Leu Cys
<210> 45
<211> 20
<212> PRT
<213> Conus circumcisus
<220>
<221> PEPTIDE
<222> (6)..(14)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
      Xaa at residues 11 and 14 is Glu or
      gamma-carboxy-Glu.
<400> 45
Gly Cys Cys Ser Asn Xaa Val Cys His Val Xaa His Xaa Xaa Leu Cys
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Arg Arg Arg Arg
<210> 46
<211> 18
<212> PRT
<213> Conus sulcatus
<220>
<221> PEPTIDE
<222> (7)..(15)
<223> Xaa at residues 7, 12 and 14 is Pro or
      hydroxy-Pro; Xaa at residue 11 is Lys,
      N-methyl-Lys, N, N-dimethyl-Lys or
      N, N, N-trimethyl-Lys; Xaa at residue 15 is Glu or
      gamma-carboxy-Glu.
<400> 46
Gly Gly Cys Cys Ser Phe Xaa Ala Cys Arg Xaa Xaa Arg Xaa Xaa Met
Cys Gly
<210> 47
<211> 18
<212> PRT
<213> Conus textile
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
Xaa at residues 2 and 15 is Glu or
      gamma-carboxy-Glu.
<400> 47
Xaa Xaa Cys Cys Ser Asp Xaa Arg Cys Asn Ser Ser His Xaa Xaa Leu
Cys Arg
<210> 48
<211> 18
<212> PRT
<213> Conus dalli
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 48
Xaa Gln Cys Cys Ser Asp Xaa Arg Cys Asn Val Gly His Xaa Xaa Leu
Cys Gly
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<210> 49
<211> 18
<212> PRT
<213> Conus dalli
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residue 1 is Gln or pyro-Glu; Xaa at
      residues 7 and 14 is Pro or hydroxy-Pro; Xaa at
      residue 15 is Glu or gamma-carboxy-Glu.
<400> 49
Xaa Val Cys Cys Ser Asp Xaa Arg Cys Asn Val Gly His Xaa Xaa Ile
Cys Gly
<210> 50
<211> 16
<212> PRT
<213> Conus textile
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6, 7 and 13 is Pro or hydroxy-Pro.
<400> 50
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<210> 51
<211> 18
<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1 and 14 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Glu or gamma-carboxy-Glu.
<400> 51
Xaa Gln Cys Cys Ser His Leu Ala Cys Asn Val Asp His Xaa Xaa Ile
Cys Arg
<210> 52
<211> 19
<212> PRT
<213> Conus sulcatus
<220>
<221> PEPTIDE
<222> (5)..(14)
<223> Xaa at residue 5 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
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Cys Arg Gln Arg

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nitro-Tyr; Xaa at residue 13 is Pro or
      hydroxy-Pro; Xaa at residue 14 is Glu or
      gamma-carboxy-Glu.
<220>
<221> PEPTIDE
<222> (18)
<223> Xaa at residue 18 is Trp or halo-Trp.
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Gly Xaa Arg
<210> 53
<211> 18
<212> PRT
<213> Conus sulcatus
<220>
<221> PEPTIDE
<222> (11)..(12)
<223> Xaa at residue 11 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys; Xaa at
      residue 12 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<220>
<221> PEPTIDE
<222> (14)..(15)
<223> Xaa at residue 14 is Pro or hydroxy-Pro; Xaa at
      residue 15 is Glu or gamma-carboxy-Glu.
Gly Gly Cys Cys Ser Phe Ala Ala Cys Arg Xaa Xaa Arg Xaa Xaa Met
Cys Gly
<210> 54
<211> 20
<212> PRT
<213> Conus sulcatus
<220>
<221> PEPTIDE
<222> (7)..(15)
<223> Xaa at residue 7 is Pro or hydroxy-Pro; Xaa at
      residue 10 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
nitro-Tyr; Xaa at residue 15 is Glu or
      gamma-carboxy-Glu.
<400> 54
Gly Gly Cys Cys Phe His Xaa Val Cys Xaa Ile Asn Leu Leu Xaa Met
```

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<210> 55
<211> 19
<212> PRT
<213> Conus betulinus
<220>
<221> PEPTIDE
<222> (7)..(15)
<223> Xaa at residues 7, 11 and 14 is Tyr, nor-Tyr,
     mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,
      O-phospho-Tyr; Xaa at residues 8, 9 and 15 is Pro
      or hydroxy-Pro.
<220>
<221> PEPTIDE
<222> (12)..(16)
<223> Xaa at residues 12 and 16 is Glu or
     gamma-carboxy-Glu.
<400> 55
Ser Ala Thr Cys Cys Asn Xaa Xaa Xaa Cys Xaa Xaa Thr Xaa Xaa Xaa
Ser Cys Leu
<210> 56
<211> 17
<212> PRT
<213> Conus betulinus
<220>
<221> PEPTIDE
<222> (5)..(13)
<223> Xaa at residues 5 and 12 is Tyr, no-Tyr,
      mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,
      O-phospho-Tyr or nitro-Tyr; Xaa at residues 6, 7
      and 13 is Pro or hydroxy-Pro.
<220>
<221> PEPTIDE
<222> (10)..(14)
<223> Xaa at residues 10 and 14 is Glu or
      gamma-carboxy-Glu.
<400> 56
Ala Cys Cys Ala Xaa Xaa Xaa Cys Phe Xaa Ala Xaa Xaa Arg Cys
Leu
<210> 57
<211> 19
<212> PRT
<213> Conus betulinus
<221> PEPTIDE
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<222> (3)..(16)
<223> Xaa at residues 3, 12 and 16 is Glu or
     gamma-carboxy-Glu; Xaa at residues 6, 7, 11 and 14
      is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr,
     O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr.
<220>
<221> PEPTIDE
<222> (8)..(15)
<223> Xaa at residues 8, 9 and 15 is Pro or hydroxy-Pro.
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Ile Cys Leu
<210> 58
<211> 227
<212> DNA
<213> Conus magus
<220>
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ttc cct tca gat cgt gca tct gat ggc agg aat gcc gca gcc aac gac
Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp
aaa gcg tot gac gtg atc acg ctg gcc ctc aag gga tgc tgt tcc aac
Lys Ala Ser Asp Val Ile Thr Leu Ala Leu Lys Gly Cys Cys Ser Asn
                                                                   189
cct gtc tgt cac ttg gag cat tca aac ctt tgt ggt aga aga cgc
Pro Val Cys His Leu Glu His Ser Asn Leu Cys Gly Arg Arg Arg
tgatgctcca ggaccctctg aaccacgacg ttcgagca
                                                                   227
<210> 59
<211> 63
<212> PRT
<213> Conus magus
<400> 59
Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser
Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp
Lys Ala Ser Asp Val Ile Thr Leu Ala Leu Lys Gly Cys Cys Ser Asn
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Pro Val Cys His Leu Glu His Ser Asn Leu Cys Gly Arg Arg Arg

<400> 62

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<210> 60
<211> 208
<212> DNA
<213> Conus aulicus
<220>
<221> CDS
<222> (1)..(168)
<400> 60
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ttc act tca gat cgt gca tct gat ggc agg aag gac gca gcg tct ggc
Phe Thr Ser Asp Arg Ala Ser Asp Gly Arg Lys Asp Ala Ala Ser Gly
ctg atc gct ctg acc atc aag gga tgc tgt tct tat cct ccc tgt ttc Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser Tyr Pro Pro Cys Phe
                                                                                    144
gcg act aat tca gac tat tgt ggt tgacgacgct gatgctccag gaccctctga
Ala Thr Asn Ser Asp Tyr Cys Gly
accacgacgt
                                                                                    208
<210> 61
<211> 56
<212> PRT
<213> Conus aulicus
<400> 61
Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser
Phe Thr Ser Asp Arg Ala Ser Asp Gly Arg Lys Asp Ala Ala Ser Gly
Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser Tyr Pro Pro Cys Phe
Ala Thr Asn Ser Asp Tyr Cys Gly
<210> 62
<211> 205
<212> DNA
<213> Conus aulicus
<220>
<221> CDS
<222> (1)..(174)
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1.0

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									agg Arg							96
									tgt Cys							144
			cca Pro						cgc Arg	tgat	get	cca (ggac	cctct	g	194
aacc	acga	icg t	t													205
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Leu	Ile	Ala 35	Leu	Thr	Met	Lys	Gly 40	Cys	Cys	Ser	Tyr	Pro 45	Pro	Cys	Phe	
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ttc Phe	tct Ser	tca Ser	ggt Gly 20	cgt Arg	agt Ser	aca Thr	ttt Phe	cgt Arg 25	ggc Gly	agg Arg	aat Asn	gcc Ala	gca Ala 30	gcc Ala	aaa Lys	96
gcg Ala	tct Ser	ggc Gly 35	Leu	gtc Val	agt Ser	ctg Leu	act Thr 40	gac Asp	agg Arg	aga Arg	cca Pro	gaa Glu 45	tgc Cys	tgt Cys	agt Ser	144
gat Asp	cct Pro 50	cgc Arg	tgt Cys	aac Asn	tcg Ser	agt Ser 55	cat His	cca Pro	gaa Glu	ctt Leu	tgt Cys 60	Gly	gga Gly	aga Arg	ege Arg	192
tga	tgct	cca	ggac	cctc	tg a	acca	cgac	g t								223

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<213> Conus textile
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Asp Pro Arg Cys Asn Ser Ser His Pro Glu Leu Cys Gly Gly Arg Arg
<210> 66
<211> 244
<212> DNA
<213> Conus textile
<220>
<221> CDS
<222> (1)..(168)
<400> 66
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Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Ala Val Val Ser
ttc act tca gat cgt gca tct gat gac ggg aaa gcc gct gcg tct gac
Phe Thr Ser Asp Arg Ala Ser Asp Asp Gly Lys Ala Ala Ala Ser Asp
ctg atc act ctg acc atc aag gga tgc tgt tct cgt cct ccc tgt atc Leu Ile Thr Leu Thr Ile Lys Gly Cys Cys Ser Arg Pro Pro Cys Ile
                                                                           144
gog aat aat oca gac ttg tgt ggt tgacgacget gatgetecag aacggtetga
Ala Asn Asn Pro Asp Leu Cys Gly
accacgacgt togagcaatg ttcaccgtgt ttctgttggt tgtctt
<210> 67
<211> 56
<212> PRT
<213> Conus textile
<400> 67
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Phe Thr Ser Asp Arg Ala Ser Asp Asp Gly Lys Ala Ala Ala Ser Asp
Leu Ile Thr Leu Thr Ile Lys Gly Cys Cys Ser Arg Pro Pro Cys Ile
Ala Asn Asn Pro Asp Leu Cys Gly
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gcg tot ggc ctg gtc agt ctg act gac agg aga cca caa tgc tgt tot Ala Ser Gly Leu Val Ser Leu Thr Asp Arg Arg Pro Gln Cys Cys Ser $\frac{35}{40}$	144
cat cct gcc tgt aac gta gat cat cca gaa att tgt cgt tgaagacgct His Pro Ala Cys Asn Val Asp His Pro Glu Ile Cys Arg 550	193
gatgeteeag gaceetetga accaegaegt	223
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Ala Ser	Gly 35	Leu	Val	Ser	Leu	Thr 40	Asp	Arg	Arg	Pro	Glu 45	Суз	Cys	Ser	
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ttc act Phe Thr															96
gcg tct Ala Ser	ggc Gly 35	Leu	gtc Val	agt Ser	ctg Leu	act Thr 40	gac Asp	agg Arg	aga Arg	cca Pro	caa Gln 45	tgc Cys	tgt Cys	tct Ser	144
cat cct His Pro 50	Āla										Asp		agac	get	193
gatgctc	cag	gacc	ctct	ga a	ccac	gacg	t								223

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			gat Asp 20													9
aaa Lys	gcg Ala	tct Ser 35	gac Asp	ctg Leu	gtc Val	gct Ala	ctg Leu 40	acc Thr	gtc Val	aag Lys	gga Gly	tgc Cys 45	tgt Cys	tct Ser	cat His	1
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gat	gete	cag ·	gacce	etet	ga ac	cac	gacgt	te	gagca	a						2:
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Lys	Ala	Ser 35	Asp	Leu	Val	Ala	Leu 40	Thr	Val	Lys	Gly	Cys 45	Cys	Ser	His	
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						acgc										

<211> 174

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Cys Gly
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<212> DNA
<213> Conus bandanus
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Val Thr Leu Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala
aaa acg cot ego ctg ate geg coa tto atc agg gat tat tgc tgt cat
                                                                      144
Lys Thr Pro Arg Leu Ile Ala Pro Phe Ile Arg Asp Tyr Cys Cys His
aga ggt ccc tgt atg gta tgg tgt ggt tgaageeget getgeteeag Arg Gly Pro Cys Met Val Trp Cys Gly
                                                                      191
                                                                      206
gaccetetga accac
<210> 81
<211> 57
<212> PRT
<213> Conus bandanus
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 Val Thr Leu Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala
 Lys Thr Pro Arg Leu Ile Ala Pro Phe Ile Arg Asp Tyr Cys Cys His
 Arg Gly Pro Cys Met Val Trp Cys Gly
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<220>
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tto act toa gat ogt got tot gat ggo agg aat goo goa goo aac gog
Phe Thr Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala
ttt gac etg ate get etg ate gee agg caa aat tge tgt age att eee
Phe Asp Leu Ile Ala Leu Ile Ala Arg Gln Asn Cys Cys Ser Ile Pro
ago tgt tgg gag aaa tat aaa tgt agt taa
                                                                   174
Ser Cys Trp Glu Lys Tyr Lys Cys Ser
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Phe Thr Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala 20 25 30
Phe Asp Leu Ile Ala Leu Ile Ala Arg Gln Asn Cys Cys Ser Ile Pro
Ser Cys Trp Glu Lys Tyr Lys Cys Ser
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<211> 219
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<213> Conus caracteristicus
<220>
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ttc act tca gat cgt gcg tct gaa ggc agg aat gct gca gcc aag gac
Phe Thr Ser Asp Arg Ala Ser Glu Gly Arg Asn Ala Ala Ala Lys Asp
aaa geg tet gae etg gtg get etg aca gte agg gga tge tgt gee att
Lys Ala Ser Asp Leu Val Ala Leu Thr Val Arg Gly Cys Cys Ala Ile
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35	4	40	45	
cgt gaa tgt cgc : Arg Glu Cys Arg : 50	ttg cag aat go Leu Gln Asn Al 55	ca gcg tat t la Ala Tyr (gt ggt gga ata Cys Gly Gly Ile 60	tac 189 Tyr
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Phe Thr Ser Asp	Arg Ala Ser G	lu Gly Arg 2 25	Asn Ala Ala Ala 30	Lys Asp
Lys Ala Ser Asp 35		eu Thr Val . 40	Arg Gly Cys Cy: 45	; Ala Ile
Arg Glu Cys Arg 50	Leu Gln Asn A 55	ala Ala Tyr	Cys Gly Gly Ile 60	: Tyr
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ttc cct tca gat Phe Pro Ser Asp 20	att gca act g Ile Ala Thr G	gag ggc agg Glu Gly Arg 25	aat gee gea ge Asn Ala Ala Al 3	a Lys Ala
ttt gac ctg ata Phe Asp Leu Ile 35	tet teg ate g Ser Ser Ile V	gtc aag aaa Val Lys Lys 40	gga tgc tgt tc Gly Cys Cys Se 45	c cat cct 144 r His Pro
gcc tgt tcg ggg Ala Cys Ser Gly 50	aat aat cca c Asn Asn Pro C	gaa ttt tgt Glu Phe Cys	cgt caa ggt cg Arg Gln Gly Ar 60	c 189
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And the gas and the control of the c

<213> Conus sulcatus

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38 30 ata gcg tct gac aag atc gct tcg acc ctc agg aga gga tgc tgt 144 Ile Ala Ser Asp Lys Ile Ala Ser Thr Leu Arg Arg Gly Gly Cys Cys 192 226 cgc tgatgctcca ggaccetetg aaccacgacg t Arg 65 <210> 93 <211> 65 <212> PRT <213> Conus sulcatus <400> 93 Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser Phe Asn Ser Asp Arg Asp Pro Ala Leu Gly Gly Arg Asn Ala Ala Ala Ile Ala Ser Asp Lys Ile Ala Ser Thr Leu Arg Arg Gly Gly Cys Cys Ser Phe Pro Ala Cys Arg Lys Tyr Arg Pro Glu Met Cys Gly Gly Arg Arg 65 <210> 94 <211> 211 <212> DNA <213> Conus sulcatus <220> <221> CDS <222> (1)..(180) <400> 94 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca gat cat gaa tct gat cgc ggt gat gcc caa acc atc caa Phe Thr Ser Asp His Glu Ser Asp Arg Gly Asp Ala Gln Thr Ile Gln 20 $\,$ 25 $\,$ 30 gaa gtg ttt gag atg ttc gct ctg gac agc gat gga tgc tgt tgg cat Glu Val Phe Glu Met Phe Ala Leu Asp Ser Asp Gly Cys Cys Trp His cet gct tgt ggc aga cac tat tgt ggt cga aga cgc tgatgctcca Pro Ala Cys Gly Arg His Tyr Cys Gly Arg Arg Arg 60 211 ggaccetetg aaccacgacg t

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189

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Arg
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65

<210> 98

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<220>

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ttc aat tca gat cgt gca tta ggt ggc agg aat gct gca gcc aaa gcg Phe Asn Ser Asp Arg Ala Leu Gly Gly Arg Asn Ala Ala Ala Lys Ala

tot gac aag atc ott tog aac otc agg aga gga tgo tgt ttt cat 144 Ser Asp Lys Ile Leu Ser Asn Leu Arg Arg Gly Gly Cys Cys Phe His

cet gte tgt tac atc aat ett eta gaa atg tgt egt caa ega gge Pro Val Cys Tyr Ile Asn Leu Leu Glu Met Cys Arg Gln Arg Gly 55

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<210> 99

<211> 63

Int Int

10

<212> PRT <213> Conus sulcatus

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Met Phe Thr Val Phe Leu Leu Val Leu Leu Ala Thr Thr Val Val Ser

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Ser Asp Lys Ile Leu Ser Asn Leu Arg Arg Gly Gly Cys Cys Phe His

Pro Val Cys Tyr Ile Asn Leu Leu Glu Met Cys Arg Gln Arg Gly

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<220>

<221> CDS

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72	
Pro Val Cys His Leu Glu His Ser Asn Met Cys Gly Arg Arg Arg 50 55 60	
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Lys Ala Ser Asp Val Ile Ala Leu Ala Leu Lys Gly Cys Cys Ser Asn 35 40 45	
Pro Val Cys His Leu Glu His Ser Asn Met Cys Gly Arg Arg Arg 50 60	
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<220> <221> CDS <222> (1)(180)	
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tcc act tca ggt ggt gca tct ggt ggc agg aag gct gca gcc aaa gcc Ser Thr Ser Gly Gly Ala Ser Gly Gly Arg Lys Ala Ala Ala Lys Ala 20 25 30	
tot aac egg ate get etg ace gte agg agt gea aca tge tgt aat tat Ser Asn Arg Ile Ala Leu Thr Val Arg Ser Ala Thr Cys Cys Asn Tys 35 40 45	144
cct ccc tgt tac gag act tat cca gaa agt tgt ctg taacgtgaat Pro Pro Cys Tyr Glu Tyr Pro Glu Ser Cys Leu 50 60 $^{5.5}$	190
catecagage titgtggetg aagacactga tgeteeagga eeetetgaac eacgaegt	248
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$<\!400>105$ Met Phe Ser Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser 1	÷
Ser Thr Ser Gly Gly Ala Ser Gly Gly Arg Lys Ala Ala Ala Lys Ala	ì

10

Ser Asn Arg Ile Ala Leu Thr Val Arg Ser Ala Thr Cys Cys Asn Tyr 40 Pro Pro Cys Tyr Glu Thr Tyr Pro Glu Ser Cys Leu <210> 106 <211> 223 <212> DNA <213> Conus betulinus <220> <221> CDS <222> (1)..(183) <400> 106 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtg gtt tcc 48 Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc act tca ggt cgt gca ttt cgt ggc agg aat cgc gca gcc gac gac Phe Thr Ser Gly Arg Ala Phe Arg Gly Arg Asn Arg Ala Ala Asp Asp 144 aaa agg tot gae otg goo got otg age gto agg gga gga tgo tgt too Lys Arg Ser Asp Leu Ala Ala Leu Ser Val Arg Gly Gly Cys Cys Ser cat cot goo tgt gog gtg aat cat coa gag ott tgt ggo tgaagaeget His Pro Ala Cys Ala Val Asn His Pro Glu Leu Cys Gly 223 gatgeeccag gaeeetetga accaegaegt <210> 107 <211> 61 <212> PRT <213> Conus betulinus <400> 107 Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser Phe Thr Ser Gly Arg Ala Phe Arg Gly Arg Asn Arg Ala Ala Asp Asp Lys Arg Ser Asp Leu Ala Ala Leu Ser Val Arg Gly Clys Cys Ser His Pro Ala Cys Ala Val Asn His Pro Glu Leu Cys Gly

<210> 108 <211> 248 <212> DNA <213> Conus betulinus

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43	
His Pro Ala Cys Ser Val Asn His Pro Glu Leu Cys Gly Arg Arg 50 $$ 55 $$ 60	Arg
tgatgcccca ggaccctctg aaccacgacg t	223
<210> 111 <211> 64 <212> PRT <213> Conus betulinus	
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Phe Thr Ser Asp Arg Ala Phe Arg Gly Arg Asn Ser Ala Ala Asn $20 \hspace{1cm} 25 \hspace{1cm} 30 \hspace{1cm}$	Asp
Lys Arg Ser Asp Leu Ala Ala Leu Ser Val Arg Arg Gly Cys Cys 35 40 45	Ser
His Pro Ala Cys Ser Val Asn His Pro Glu Leu Cys Gly Arg Arg 50 60	Arg
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tot aac cgg atc gct ctg atc gtc agg aat gca gaa tgc tgt tat Ser Asn Arg Ile Ala Leu Ile Val Arg Asn Ala Glu Cys Cys Tyt 40 45 45	t tat 144 r Tyr
oct coc tgt tac gag gct tat cca gaa att tgt ctg taacgtgaat Pro Pro Cys Tyr Glu Âla Tyr Pro Glu Ile Cys Leu 50 60	190
catccagace tttgtggetg aagaceetga tgeteeagga eeetetgaac cac	gacgt 248
<210> 113 <211> 60 <212> PRT <213> Conus betulinus	
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Phe Thr Ser Gly Arg Ala Ser Gly Gly Arg Asn Ala Ala Ala Ly	s Ala

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Ser Asn Arg Ile Ala Leu Ile Val Arg Asn Ala Glu Cys Cys Tyr Tyr 45

Pro Pro Cys Tyr Glu Ala Tyr Pro Glu Ile Cys Leu
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25

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<212> DNA <213> Conus pennaceus

<220>

<221> CDS <222> (1)..(168)

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ttc act tca gat cgt gca tct gat ggc ggg aat gcc gca gcg tct gac 96 Phe Thr Ser Asp Arg Ala Ser Asp Gly Gly Asn Ala Ala Ser Asp 20 25 30

ctg atc gct ctg acc atc aag gga tgc tgt tct cat cct ccc tgt gcc Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser His Pro Pro Cys Ala

atg aat aat cca gac tat tgt ggt tgacgacgct gatgctccag gaccctctga $\,$ 198 Met Asn Pro Asp Tyr Cys Gly $\,$

accacgacg

207

<210> 115 <211> 56

<212> PRT <213> Conus pennaceus

<400> 115

Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Ile Ser 1 5 10 15

Phe Thr Ser Asp Arg Ala Ser Asp Gly Gly Asn Ala Ala Ala Ser Asp 20 25 30

Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser His Pro Pro Cys Ala 35 40 45

Met Asn Asn Pro Asp Tyr Cys Gly
50 55

<210> 116

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<220>

<221> CDS

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ttc Phe	act Thr	tca Ser	gat Asp 20	cgt Arg	gca Ala	tct Ser	gat Asp	ggc Gly 25	ggg Gly	aat Asn	gcc Ala	gca Ala	atg Met 30	tct Ser	gac Asp	96
ctg Leu	atc Ile	gct Ala 35	ctg Leu	acc Thr	atc Ile	aag Lys	gga Gly 40	tgc Cys	tgt Cys	tct Ser	cat His	cct Pro 45	ccc Pro	tgt Cys	ttc Phe	144
ctg Leu	aat Asn 50	aat Asn	cca Pro	gac Asp	tat Tyr	tgt Cys 55	ggt Gly	tga	egac	get (gatgo	teca	ig g	accct	ctga	198
acca	cgad	g														207
	.> 50 ?> P1 3> Co	S RT onus	pen	nace	ıs											
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Phe	Thr	Ser	Asp 20	Arg	Ala	Ser	Asp	Gly 25	Gly	Asn	Ala	Ala	Met 30	Ser	Asp	
Leu	Ile	Ala 35		Thr	Ile	Lys	Gly 40		Cys	Ser	His	Pro 45	Pro	Cys	Phe	
Leu	Asn 50	Asn	Pro	Asp	Tyr	Cys 55	Gly									
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	1> C		(171	.)												
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ttc Phe	cct	tca Sei	a gat c Asp 20) Arc	gaa gGlu	tct Ser	gat Asp	gg Gly	y Ala	g aat a Asr	gac n Asp	gaa Glu	gco Ala 30	a Arç	acc Thr	96
gac Asp	gaç Glu	ect Pro	o Glu	g gaq ı Glu	g cac 1 His	gga Gly	r ccq 7 Pro	As)	e ago	g aat g Ast	gga n Gly	tgc Cys 45	: Cy:	agg Arg	g aat g Asn	14
cct	geo	tgt	t ga	g ago	c cac	c aga	a tg	gg'	t tg	acga	eget	gato	jete	cag		19

Pro Ala Cys Glu Ser His Arg Cys Gly 210 gaccctctga accacgacg <210> 119 <211> 57 <212> PRT <213> Conus stercusmuscarum <400> 119 Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser Phe Pro Ser Asp Arg Glu Ser Asp Gly Ala Asn Asp Glu Ala Arg Thr Asp Glu Pro Glu Glu His Gly Pro Asp Arg Asn Gly Cys Cys Arg Asn Pro Ala Cys Glu Ser His Arg Cys Gly <210> 120 <211> 210 <213> Conus circumcisus <221> CDS <222> (1)..(180) <400> 120 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser tto cot toa gat ogt goa tot gat ggo agg aat goo goa goo ago gac 96 Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Ser Asp aga geg tet gae geg gee cae eag gga tge tgt tee aac eet gte tgt 144 Arg Ala Ser Asp Ala Ala His Glm Gly Cys Cys Ser Asn Pro Val Cys 190 cac gtg gaa cat cca gaa ctt tgt cgt aga aga cgc tgatgctcca His Val Glu His Pro Glu Leu Cys Arg Arg Arg Arg ggaccetetg aaccacgacg <210> 121 <211> 60 <212> PRT <213> Conus circumcisus <400> 121 Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ser Asp

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<212> DNA <213> Con <220>

<221> CDS

<213> Conus episcopatus

<210> 124 <211> 207

50										
<222> (1)(168)										
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ttc act tca gat cgt gca tct gat agc agg aag gac gca gcg tct ggc Fhe Thr Ser Asp Arg Ala Ser Asp Ser Arg Lys Asp Ala Ala Ser Gly $20 \hspace{1.5cm} 25 \hspace{1.5cm} 30$	96									
ctg atc gct ctg acc atc aag gga tgc tgt tct gat cct cgc tgt aac Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser Asp Pro Arg Cys Asn $35 \hspace{1.5cm} 40 \hspace{1.5cm} 45$	144									
atg aat aat cca gac tat tgt ggt tgacgacget gatgeteeag gaccetetga Met Asn Asn Pro Asp Tyr Cys Gly $$50\ $	198									
accacgacg	207									
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Phe Thr Ser Asp Arg Ala Ser Asp Ser Arg Lys Asp Ala Ala Ser Gly 20 30										
Leu Ile Ala Leu Thr Ile Lys Gly Cys Cys Ser Asp Pro Arg Cys Asn $35 \ \ 40 \ \ $										
Met Asn Asn Pro Asp Tyr Cys Gly 50										
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aga ttg gtg tct ctc cct cag atc gcc cat gct gac tgt tgt tcc gat Arg Leu Val Ser Leu Pro Gln Ile Ala His Ala Asp Cys Cys Ser Asp 35 40 45	144									
cot god tgd aag dag acg coc ggt tgt ogt taaagacgot gotgotocag	194									

Pro Ala Cys Lys Gln Thr Pro Gly Cys Arg 213 gaccetetga accaegacg <210> 127 <211> 58 <212> PRT <213> Conus sponsalis <400> 127 Met Ser Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser Phe Thr Val Asp Arg Ala Ser Asp Gly Arg Asp Val Ala Ile Asp Asp Arg Leu Val Ser Leu Pro Gln Ile Ala His Ala Asp Cys Cys Ser Asp Pro Ala Cys Lys Gln Thr Pro Gly Cys Arg <210> 128 <211> 221 <212> DNA <213> Conus sponsalis <220> <221> CDS <222> (1)..(168) <400> 128 atg tte acc gtg ttt ctg ttg gtt gtc ttg gca acc acc gtc gct tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Ala Ser ttc att atc gat gat cca tct gat ggc agg aat att gca gtc gac gac Phe Ile Ile Asp Asp Pro Ser Asp Gly Arg Asn Ile Ala Val Asp Asp aga ggg ctt ttc tct acg ctc ttc cat gct gat tgc tgt gaa aat cct Arg Gly Leu Phe Ser Thr Leu Phe His Ala Asp Cys Cys Glu Asn Pro gcc tgt aga cac acg cag ggt tgt tgatetttgt tetteaaaga cactgetgge Ala Cys Arg His Thr Gln Gly Cys 221 ccaqqaccct ctgaaccacg acg <210> 129 <211> 56 <212> PRT <213> Conus sponsalis <400> 129 Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Ala Ser Phe Ile Ile Asp Asp Pro Ser Asp Gly Arg Asn Ile Ala Val Asp Asp

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Ser Gly Leu Val Gly Leu Thr Asp Lys Thr Arg Gly Cys Cys Ser His

Pro Ala Cys Asn Val Asp His Pro Glu Ile Cys Gly

<210> 132 <211> 208 <212> DNA <213> Conus dalli <221> CDS

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ttc Phe	act Thr	tca Ser	gat Asp 20	ggt Gly	gca Ala	tct Ser	gat Asp	gac Asp 25	agg Arg	aaa Lys	gcc Ala	gct Ala	gcg Ala 30	tct Ser	gac Asp	96
ctg Leu	atc Ile	act Thr 35	ctg Leu	acc Thr	atc Ile	aag Lys	gga Gly 40	tgc Cys	tgt Cys	tct Ser	cgt Arg	cct Pro 45	ccc Pro	tgt Cys	atc Ile	144
gcg Ala	aat Asn 50	aat Asn	cca Pro	gac Asp	ttg Leu	tgt Cys 55	ggt Gly	cga Arg	cga Arg	ege Arg	tgat	gete	ca (ggaco	eetetg	197
aaco	cacga	acg	t													208
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Phe	Thr	Ser	Asp 20	Gly	Ala	Ser	Asp	Asp 25	Arg	Lys	Ala	Ala	Ala 30	Ser	Asp	
Leu	Ile	Thr 35	Leu	Thr	Ile	Lys	Gly 40	Cys	Cys	Ser	Arg	Pro 45	Pro	Cys	Ile	
Ala	Asn 50	Asn	Pro	Asp	Leu	Cys 55	Gly	Arg	Arg	Arg						
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	1> C		(192)												
atq	Phe	acc	gtg Val	ttt Phe	Leu	ttg Leu	gtt Val	gtc Val	ttg Leu 10	Ala	acc Thr	act Thr	gtc Val	gtt Val 15	tcc Ser	48
tcc Ser	act Thr	tca Ser	ggt Gly 20	/ Arg	cgt Arg	gca Ala	ttt Phe	cat His 25	Gly	agg Arg	r aat Asn	gcc Ala	gca Ala 30	Ala	aaa Lys	96
gco Ala	tct Ser	gga Gly	/ Leu	g gto 1 Val	ggt Gly	ctg Leu	act Thr 40	Asp	agg Arg	aga Arg	cca Pro	Gln 45	. Cys	tgt Cys	agt Ser	144
gat	cct	cgo	tgt	aac	gta	ggt	cat	cca	gaa	ctt	tgt	ggt	gga	aga	e cgc	192

J 4	
Asp Pro Arg Cys Asn Val Gly His Pro Glu Leu Cys Gly Gly Arg Arg $50 \ \ $	
tgatgctcca ggaccctctg aaccacaacg t	223
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Ser Thr Ser Gly Arg Arg Ala Phe His Gly Arg Asn Ala Ala Ala Lys $$20$$	
Ala Ser Gly Leu Val Gly Leu Thr Asp Arg Arg Pro Gln Cys Cys Ser $$35$$	
Asp Pro Arg Cys Asn Val Gly His Pro Glu Leu Cys Gly Gly Arg Arg $50 \ \ $ $60 \ \ $	
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<220> <221> CDS <222> (1)(189)	
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too act toa ggt cgt gca ttt cat ggc agg aat gcc gca gcc aaa gcg Ser Thr Ser Gly Arg Ala Phe His Gly Arg Asn Ala Ala Lys Ala 20	96
tot ggc etg gtc ggt etg acc gac aag agg caa gta tgc tgt agt gat Ser Gly Leu Val Gly Leu Thr Asp Lys Arg Gln Val Cys Cys Ser Asp 45 45	144
oct ogc tgt aac gta ggt cat cca gaa att tgt ggt gga aga ogc Pro Arg Cys Asn Val Gly His Pro Glu Ile Cys Gly Gly Arg Arg 55 55	189
tgatgeteca ggaecetetg aaceaegaeg t	220
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		55		
20		25	30)
Ser Gly Leu Val	Gly Leu Thr	Asp Lys Arg (Gln Val Cys Cys 45	Ser Asp
Pro Arg Cys Asn 50	Val Gly His 55	Pro Glu Ile (Cys Gly Gly Arc	į Arg
<210> 138 <211> 208 <212> DNA <213> Conus acha	itinus			
<220> <221> CDS <222> (1)(180)				
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ttc cct tca gat Phe Pro Ser Asp 20	agt gca tct Ser Ala Ser	ggt ggc agg o Gly Gly Arg i 25	gat gac gag gco Asp Asp Glu Ala 30	a Lys Asp
gaa agg tot gac Glu Arg Ser Asp 35	atg tac gaa Met Tyr Glu	ttg aaa cgg a Leu Lys Arg a 40	aat gga cgc tg Asn Gly Arg Cy: 45	tgc cat 144 Cys His
cct gcc tgt ggt Pro Ala Cys Gly 50	ggc aaa tac Gly Lys Tyr 55	gtt aaa tgt (Val Lys Cys (gga cgc tgatgc Gly Arg 60	ccca 190
ggaccetete gaace	cacg			208
<210> 139 <211> 60 <212> PRT <213> Conus acha	atinus			
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Phe Pro Ser Asp 20	Ser Ala Ser	Gly Gly Arg . 25	Asp Asp Glu Ala	ı Lys Asp
Glu Arg Ser Asp 35	Met Tyr Glu	Leu Lys Arg	Asn Gly Arg Cy: 45	s Cys His
Pro Ala Cys Gly 50	Gly Lys Tyr 55	Val Lys Cys	Gly Arg 60	
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<220> <221> CDS

<222> (1)..(174) <400> 140 atg tto acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser ttc tct aca gat gat gaa tct gat ggc tcg aat gaa gaa ccc agc gcc Phe Ser Thr Asp Asp Glu Ser Asp Gly Ser Asn Glu Glu Pro Ser Ala gac cag act gcc agg tcc tca atg aac agg gcg cct gga tgc tgt aac Asp Gln Thr Ala Arg Ser Ser Met Asn Arg Ala Pro Gly Cys Cys Asn 40 aat oot goo tgt gtg aag cac aga tgt gga tgacgotgat gotocaggac Asn Pro Ala Cys Val Lys His Arg Cys Gly 211 cctctgaacc acgacgt <210> 141 <211> 58 <212> PRT <213> Conus bullatus <400> 141 Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser Phe Ser Thr Asp Asp Glu Ser Asp Gly Ser Asn Glu Glu Pro Ser Ala Asp Gln Thr Ala Arg Ser Ser Met Asn Arg Ala Pro Gly Cys Cys Asn Asn Pro Ala Cys Val Lys His Arg Cys Gly <210> 142 <211> 214 <212> DNA <213> Conus bullatus <220> <221> CDS <222> (1)..(177) <400> 142 atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser tto tot aca gat gat gaa tot gat ggc tog aat gaa gaa coc ago goo 96 Phe Ser Thr Asp Asp Glu Ser Asp Gly Ser Ash Glu Glu Pro Ser Ala gac cag get gee agg tee gea atg aac agg eeg eet gga tge tgt aac Asp Gin Ala Ala Arg Ser Ala Met Asn Arg Pro Pro Gly Cys Cys Asn

aat oot goo tgt gtg aag oac aga tgt ggt gga tgacgotgat gotocaggac 197

1 1.47

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<211> 59
<212> PRT
<213> Conus bullatus
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Phe Ser Thr Asp Asp Glu Ser Asp Gly Ser Asn Glu Glu Pro Ser Ala 20 \, 25 \, 30 \,
Asp Gln Ala Ala Arg Ser Ala Met Asn Arg Pro Pro Gly Cys Cys Asn
Asn Pro Ala Cys Val Lys His Arg Cys Gly Gly
<210> 144
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                                                                        48
tto cot toa gat ogt gac tot gat ggo gog gat goo gaa goo agt gac
                                                                        96
Phe Pro Ser Asp Arg Asp Ser Asp Gly Ala Asp Ala Glu Ala Ser Asp
gag cot gtt gag tto gaa agg gac gag aat gga tgo tgt tgg aat cot
Glu Pro Val Glu Phe Glu Arg Asp Glu Asn Gly Cys Cys Trp Asn Pro
          35
tee tgt eeg agg eec aga tgt aca gga ega ege taatgeteea ggaeeetetg 197
Ser Cys Pro Arg Pro Arg Cys Thr Gly Arg Arg
                                                                         208
aaccacgacg t
<210> 145
<211> 59
<212> PRT
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Phe Pro Ser Asp Arg Asp Ser Asp Gly Ala Asp Ala Glu Ala Ser Asp
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<210> 146 <211> 211

Ser Cys Pro Arg Pro Arg Cys Thr Gly Arg Arg 50

Glu Pro Val Glu Phe Glu Arg Asp Glu Asn Gly Cys Cys Trp Asn Pro

30

cct ccc tgt gct gtg ctg tat tgt ggt aga aga cgc tgatgctcca Pro Pro Cys Ala Val Leu Tyr Cys Gly Arg Arg Arg 190

211

Met Phe Thr Val Phe Leu Leu Val Val Leu Thr Thr Thr Val Val Ser

Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp

Lys Ala Ser Asp Val Val Thr Leu Val Leu Lys Gly Cys Cys Ser Thr

Pro Pro Cys Ala Val Leu Tyr Cys Gly Arg Arg Arg

<210> 148 <211> 212

<212> DNA <213> Conus distans

<220> <221> CDS

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gat cgt gca tct tat ggc agg tat gcc tca ccc gtc gac aga gcg tct Asp Arg Ala Ser Tyr Gly Arg Tyr Ala Ser Pro Val Asp Arg Ala Ser 20 25 30	96
gcc ctg atc gct cag gcc atc ctt cga gat tgc tgc tcc aat cct cct Ala Leu Ile Ala Gln Ala Ile Leu Arg Asp Cys Cys Ser Asn Pro Pro $\frac{35}{40} \qquad \qquad \frac{45}{45}$	144
tgt gcc cat aat aat cca gac tgt cgt taaaagacgct gcttgctcca Cys Ala His Asn Asn Pro Asp Cys Arg 50 55	191
ggaccctctg aaccacgacg t	212
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Met Phe Thr Val Phe Leu Leu Val Val Phe Ala Ser Ser Val Thr Leu 1 10 15	
Asp Arg Ala Ser Tyr Gly Arg Tyr Ala Ser Pro Val Asp Arg Ala Ser $20 \\ 25 \\ 30$	
Ala Leu Ile Ala Gln Ala Ile Leu Arg Asp Cys Cys Ser Asn Pro Pro 35 $$40$$	
Cys Ala His Asn Asn Pro Asp Cys Arg 50 55	
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<220> <221> CDS <222> (1)(60)	
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ggt gga aga cgc tga Gly Gly Arg Arg 20	63
<210> 151 <211> 20 <212> PRT <213> Conus textile	

<221> PEPTIDE <222> (4)..(12)

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Gly Gly Arg Arg
<210> 152
<211> 220
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<213> Conus consors
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Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp
aaa gog tot gae gtg atc acg ctg goo otc aag gga tgc tgt toc aac
                                                                   144
Lys Ála Ser Ásp Val Ile Thr Leu Ála Leu Lys Gly Cys Cys Ser Asn
         35
oot gto tgt cao ttg gag cat toa aac ott tgt ggt aga aga ogo
Pro Val Cys His Leu Glu His Ser Asn Leu Cys Gly Arg Arg Arg
     50
tgatgeteca ggaccetetg aaccaegaeg t
<210> 153
<211> 63
<212> PRT
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Phe Pro Ser Asp Arg Ala Ser Asp Gly Arg Asn Ala Ala Asn Asp
Lys Ala Ser Asp Val Ile Thr Leu Ala Leu Lys Gly Cys Cys Ser Asn
 Pro Val Cys His Leu Glu His Ser Asn Leu Cys Gly Arg Arg Arg
      50
 <210> 154
 <211> 15
 <212> PRT
 <213> Conus musicus
```

<222> (4)..(13)

<223> Xaa at residues 4 and 13 is Tyr, nor-Tyr,

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<223> Xaa at residues 4, 11 and 12 is Tyr, nor-Tyr,
      mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,
      O-phospho-Tyr or nitro-Tyr. Xaa at residue 6 is
      Pro or hydroxy-Pro.
<221> PEPTIDE
<222> (9)..(15)
<223> Xaa at residues 9, 10 and 15 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys; Xaa at
      residue 14 is Trp (D or L) or halo-Trp.
<400> 154
Gly Cys Cys Xaa Asn Xaa Val Cys Xaa Xaa Xaa Xaa Cys Xaa Xaa
<210> 155
<211> 16
<212> PRT
<213> Conus purpurascens
<220>
<221> PEPTIDE
<222> (1)..(3)
<223> Xaa at residue 1 is Gln or pyro-Glu; Xaa at
      residue 2 is Glu or gamma-carboxy-Glu; Xaa at
      residues 3 and 9 is Pro or hydroxy-Pro.
<221> PEPTIDE
<222> (13)
<223> Xaa at residue 13 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 155
Xaa Xaa Xaa Gly Cys Cys Arg His Xaa Ala Cys Gly Xaa Asn Arg Cys
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<210> 156
<211> 13
<212> PRT
<213> Conus musicus
<220>
<221> PEPTIDE
<222> (5)..(11)
<223> Xaa at residues 5 and 11 is Pro or hydroxy-Pro.
<400> 156
Cys Cys Ala Asp Xaa Asp Cys Arg Phe Arg Xaa Gly Cys
<210> 157
<211> 17
<212> PRT
<213> Conus musicus
<220>
<221> PEPTIDE
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mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr; Xaa at residues 6 and 10 is Pro or hydroxy-Pro. <221> PEPTIDE <222> (9)..(17) <223> Xaa at residues 9 and 16 is Trp (D or L) or halo-Trp; Xaa at residues 11 and 17 is Lys, N-methyl-Lys, N, N-dimethyl-Lys or N, N, N-trimethyl-Lys. <400> 157 Gly Cys Cys Xaa Asn Xaa Ser Cys Xaa Xaa Xaa Thr Xaa Cys Ser Xaa Xaa <210> 158 <211> 13 <212> PRT <213> Conus musicus <220> <221> PEPTIDE <222> (5)..(8) <223> Xaa at residue 5 is Pro or hydroxy-Pro; Xaa at residue 8 is Lys, N-methyl-Lys, N,N-dimethyl-Lys or N, N, N-trimethyl-Lys. <220> <221> PEPTIDE <222> (9)..(11) <223> Xaa at residue 9 is Glu or gamma-carboxy-Glu; Xaa at residue 11 is Tyr, nor-Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tvr. <400> 158 Cys Cys Ser Asn Xaa Thr Cys Xaa Xaa Thr Xaa Gly Cys <210> 159 <211> 13 <212> PRT <213> Conus musicus <220> <221> PEPTIDE <222> (5)..(11) <223> Xaa at residues 5 and 11 is Pro or hydroxy-Pro; Xaa at residue 8 is Lys, N-methyl-Lys, N. N-dimethyl-Lys or N. N. N-trimethyl-Lys. <400> 159 Cys Cys Ala Asn Xaa Ile Cys Xaa Asn Thr Xaa Gly Cys

<210> 160 <211> 13

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<212> PRT
<213> Conus musicus
<220>
<221> PEPTIDE
<222> (5)..(8)
<223> Xaa at residue 5 is Pro or hydroxy-Pro; Xaa at
      residue 8 is Lys, N-methyl-Lys, N,N-dimethyl-Lys
      or N.N.N-trimethyl-Lys.
<220>
<221> PEPTIDE
<222> (9)..(11)
<223> Xaa at residue 9 is Glu or gamma-carboxy-Glu; Xaa
      at residue 11 is Tyr, mono-halo-Tyr, di-halo-Tyr,
      O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr.
<400> 160
Cys Cys Asn Asn Xaa Thr Cys Xaa Xaa Thr Xaa Gly Cys
<210> 161
<211> 13
<212> PRT
<213> Conus musicus
<220>
<221> PEPTIDE
<222> (5)..(8)
<223> Xaa at residue 5 is Pro or hydroxy-Pro; Xaa at
      residue 8 is Lys, N-methyl-Lys, N,N-dimethyl-Lys
      or N, N, N-trimethyl-Lys.
<220>
<221> PEPTIDE
<222> (9)..(11)
<223> Xaa at residue 9 is Glu or gamma-carboxy-Glu; Xaa
      at residue 11 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 161
Cys Cys Ser Asn Xaa Val Cys Xaa Xaa Thr Xaa Gly Cys
<210> 162
<211> 17
<212> PRT
<213> Conus betulinus
<220>
<221> PEPTIDE
<222> (6)..(14)
<223> Xaa at residue 6 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr; Xaa at residues 7, 8 and 14 is Pro or
      hvdroxv-Pro.
<220>
<221> PEPTIDE
<222> (15)
<223> Xaa at residue 15 is Lys, N-methyl-Lys,
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N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.

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<400> 162
Gly Gly Cys Cys Ser Xaa Xaa Xaa Cys Ile Ala Ser Asn Xaa Xaa Cys
Gly
<210> 163
<211> 15
<212> PRT
<213> Conus lividus
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 163
Gly Cys Cys Ser His Xaa Val Cys Ser Ala Met Ser Xaa Ile Cys
<210> 164
<211> 15
<212> PRT
<213> Conus musicus
<220>
<221> PEPTIDE
<222> (4)..(12)
<223> Xaa at residues 4 and 12 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys; Xaa at
      residue 6 is Pro or hydroxy-Pro.
<221> PEPTIDE
<222> (7)..(14)
<223> Xaa at residues 7 and 14 is Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 164
Gly Cys Cys Xaa Asn Xaa Xaa Cys Gly Ala Ser Xaa Thr Xaa Cys
<210> 165
<211> 15
<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (5)..(13)
<223> Xaa at residue 5 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-nalo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr; Xaa at residues 6, 7 and 13 is Pro or
      hydroxy-Pro.
<400> 165
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Gly Cys Cys Ser Xaa Xaa Xaa Cys Phe Ala Thr Asn Xaa Asp Cys

15

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<220>
                                <221> PEPTIDE
                                 <222> (6)..(14)
                                 <223> Xaa at residue 6 is Tyr, nor-Tyr, mono-halo-Tyr,
                                                       di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
                                                       nitro-Tyr; Xaa at residues 7, 8 and 14 is Pro or
                                                       hydroxy-Pro.
                                 <400> 166
                                Gly Gly Cys Cys Ser Xaa Xaa Xaa Cys Ile Ala Asn Asn Xaa Leu Cys
The state of the s
                                Ala
                                <210> 167
                                <211> 17
                                 <212> PRT
                                <213> Conus radiatus
100
                                 <220>
                                 <221> PEPTIDE
1000
                                 <222> (6)..(14)
                                 <223> Xaa at residue 6 is Tyr, nor-Tyr, mono-halo-Tyr,
                                                       di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
                                                        nitro-Tyr; Xaa at residues 7, 8 and 14 is Pro or
                                                       hydroxy-Pro.
                                 <400> 167
                                 Gly Gly Cys Cys Ser Xaa Xaa Xaa Cys Ile Ala Asn Asn Xaa Phe Cys
                                 Ala
                                  <210> 168
                                  <211> 16
                                  <212> PRT
                                  <213> Conus virgo
                                  <220>
                                  <221> PEPTIDE
                                  <222> (6)..(13)
                                  <223> Xaa at residues 6, 7 and 13 is Pro or hydroxy-Pro.
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Asp Cys Cys Ser Asn Xaa Xaa Cys Ser Gln Asn Asn Xaa Asp Cys Met

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<210> 166 <211> 17 <212> PRT <213> Conus radiatus

<400> 168

<210> 169 <211> 16 <212> PRT <213> Conus virgo

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<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6, 7 and 13 is Pro or hydroxy-Pro.
<400> 169
Asp Cys Cys Ser Asn Xaa Xaa Cys Ala His Asn Asn Xaa Asp Cys Arg
<210> 170
<211> 20
<212> PRT
<213> Conus achatinus
<220>
<221> PEPTIDE
<222> (1)..(14)
<223> Xaa at residues 1, 11 and 14 is Glu or
      gamma-carboxy-Glu; Xaa at residue 6 is Pro or
      hydroxy-Pro.
<400> 170
Xaa Cys Cys Thr Asn Xaa Val Cys His Ala Xaa His Gln Xaa Leu Cys
Ala Arg Arg Arg
<210> 171
<211> 16
<212> PRT
<213> Conus achatinus
<220>
<221> PEPTIDE
<222> (6)..(10)
<223> Xaa at residue 6 is Pro or hydroxy-Pro; Xaa at
      residue 10 is Glu or gamma-carboxy-Glu.
<400> 171
Gly Cys Cys Ser Asn Xaa Val Cys His Leu Xaa His Ser Asn Leu Cys
<210> 172
<211> 20
<212> PRT
<213> Conus achatinus
<220>
<221> PEPTIDE
<222> (1)..(14)
<223> Xaa at residues 1, 11 and 14 is Glu or
      gamma-carboxy-Glu; Xaa at residue 6 is Pro or
      hydroxy-Pro.
Xaa Cys Cys Thr Asn Xaa Val Cys His Val Xaa His Gln Xaa Leu Cys
Ala Arg Arg Arg
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<210> 173
<211> 17
<212> PRT
<213> Conus ammiralis
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residue 1 is Gln or pyro-Glu; Xaa at
      residues 2 and 15 is Glu or gamma-carboxy-Glu; Xaa
      at residue 6 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<221> PEPTIDE
<222> (7)..(14)
<223> Xaa at residues 7 and 14 is Pro or hydroxy-Pro.
<400> 173
Xaa Xaa Cys Cys Ser Xaa Xaa Ala Cys Asn Leu Asp His Xaa Xaa Leu
<210> 174
<211> 18
<212> PRT
<213> Conus ammiralis
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residues 1, 7 and 14 is Pro or hydroxy-Pro;
    Xaa at residues 2 and 15 is Glu or
      gamma-carboxy-Glu.
<400> 174
Xaa Xaa Cys Cys Ser Asp Xaa Arg Cys Asn Ser Thr His Xaa Xaa Leu
Cys Gly
<210> 175
<211> 21
<212> PRT
<213> Conus arenatus
<220>
<221> PEPTIDE
<222> (7)..(12)
 <223> Xaa at residues 7 and 8 is Pro or hydroxy-Pro; Xaa
       at residue 10 is Trp (D or L) or halo-Trp; Xaa at
       residues 11 and 12 is Lys, N-methyl-Lys,
       N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
 <221> PEPTIDE
 <222> (13)..(19)
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<223> Xaa at residue 13 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr ; Xaa at residue 19 is Glu or
      gamma-carboxy-Glu.
<400> 175
Leu Asn Cys Cys Met Ile Xaa Xaa Cys Xaa Xaa Xaa Xaa Gly Asp Arg
Cys Ser Xaa Val Arg
<210> 176
<211> 22
<212> PRT
<213> Conus arenatus
<220>
<221> PEPTIDE
<222> (9)..(20)
<223> Xaa at residue 9 is Pro or hydroxy-Pro; Xaa at
      residues 12 and 20 is Glu or gamma-carboxy-Glu;
      Xaa at residue 14 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 176
Ala Phe Gly Cys Cys Asp Leu Ile Xaa Cys Leu Xaa Arg Xaa Gly Asn
Arg Cys Asn Xaa Val His
<210> 177
<211> 21
<212> PRT
<213> Conus arenatus
<220>
<221> PEPTIDE
<222> (8)..(16)
<223> Xaa at residue 8 is Pro or hydroxy-Pro; Xaa at
      residue 10 is Trp (D or L) or halo-Trp; Xaa at
      residues 12 and 16 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<221> PEPTIDE
<222> (11)..(19)
<223> Xaa at residues 11 and 19 is Glu or
      gamma-carboxy-Glu; Xaa at residue 13 is Tyr,
      mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,
      O-phospho-Tyr or nitro-Tyr.
<400> 177
Leu Gly Cys Cys Asn Val Thr Xaa Cys Xaa Xaa Xaa Xaa Gly Asp Xaa
Cys Asn Xaa Val Arg
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<210> 178
<211> 20
<212> PRT
<213> Conus arenatus
<220>
<221> PEPTIDE
<222> (2)..(14)
<223> Xaa at residue 2 is Glu or gamma-carboxy-Glu; Xaa
      at residues 7 and 14 is Pro or hydroxy-Pro.
<400> 178
Asp Xaa Cys Cys Ser Asn Xaa Ala Cys Arg Val Asn Asn Xaa His Val
Cys Arg Arg Arg
<210> 179
<211> 21
<212> PRT
<213> Conus arenatus
<220>
<221> PEPTIDE
<222> (7)..(12)
<223> Xaa at residue 7 is Pro or hydroxy-Pro; Xaa at
      residue 10 is Trp (D or L) or halo-Trp; Xaa at
      residue 12 is Glu or gamma-carboxy-Glu.
<220>
<221> PEPTIDE
<222> (13)..(19)
<223> Xaa at residue 13 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
       nitro-Tyr, Xaa at residues 14 and 19 is Lys,
      N-methyl-Lys, N,N-dimethyl-Lys or
      N.N.N-trimethyl-Lys.
<400> 179
Leu Asn Cys Cys Ser Ile Xaa Gly Cys Xaa Asn Xaa Xaa Asp Arg
Cys Ser Xaa Val Arg
              20
<210> 180
<211> 18
<212> PRT
<213> Conus aurisiacus
<220>
<221> PEPTIDE
 <222> (7)..(14)
 <223> Xaa at residues 7 and 14 is Pro or hydroxy-Pro;
       Xaa at residue 10 is Tyr, mono-halo-Tyr,
       di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
       nitro-Tyr.
 <400> 180
 Gly Gly Cys Cys Ser His Xaa Val Cys Xaa Phe Asn Asn Xaa Gln Met
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Cys Arg <210> 181 <211> 18 <212> PRT <213> Conus aurisiacus <220> <221> PEPTIDE <222> (7)..(14) <223> Xaa at residues 7 and 14 is Pro or hydroxy-Pro. <400> 181 Gly Gly Cys Cys Ser His Xaa Val Cys Asn Leu Asn Asn Xaa Gln Met Cys Arg <210> 182 <211> 17 <212> PRT <213> Conus bandanus <220> <221> PEPTIDE <222> (6)..(15) <223> Xaa at residues 6 and 7 is Pro or hydroxy-Pro; Xaa at residues 9 and 15 is Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr. <400> 182 Gly Cys Cys Ser His Xaa Xaa Cys Xaa Ala Asn Asn Gln Ala Xaa Cys Asn <210> 183 <211> 17 <212> PRT <213> Conus betulinus <220> <221> PEPTIDE <222> (7)..(15) <223> Xaa at residues 7 and 14 is Pro and hydroxy-Pro; Xaa at residue 15 is Glu or gamma-carboxy-Glu. <400> 183 Gly Gly Cys Cys Ser His Xaa Ala Cys Ser Val Thr His Xaa Xaa Leu Cys

<210> 184 <211> 18

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<212> PRT
<213> Conus betulinus
<220>
<221> PEPTIDE
<222> (6)..(12)
<223> Xaa at residue 6 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr; Xaa at residue 7 is Pro and
      hydroxy-Pro; Xaa at residue 12 is Glu or
      gamma-carboxy-Glu.
<400> 184
Gly Gly Cys Cys Ser Xaa Xaa Ala Cys Ser Val Xaa His Gln Asp Leu
Cys Asp
<210> 185
<211> 25
<212> PRT
<213> Conus caracteristicus
<220>
<221> PEPTIDE
<222> (8)..(22)
<223> Xaa at residues 8 and 22 is Pro or hydroxy-Pro;
      Xaa at residue 10 is Trp (D or L) or halo-Trp; Xaa
      at residue 13 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<220>
<221> PEPTIDE
<222> (15)..(19)
<223> Xaa at residues 15, 16 and 19 is Glu or
      gamma-carboxy-Glu.
<400> 185
Val Ser Cys Cys Val Val Arg Xaa Cys Xaa Ile Arg Xaa Gln Xaa Xaa
Cys Leu Xaa Ala Asp Xaa Arg Thr Leu
             20
<210> 186
<211> 21
<212> PRT
<213> Conus caracteristicus
<220>
<221> PEPTIDE
<223> Xaa at residue 1 is Gln or pyro-Glu; Xaa at
      residue 7 is Pro or hydroxy-Pro; Xaa at residue 10
       is Trp (D or L) or halo-Trp; Xaa at residues 11
      and 19 is Glu or gamma-carboxy-Glu.
<220>
<221> PEPTIDE
<222> (12)..(16)
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<223> Xaa at residues 12 and 16 is Lys, N-methyl-Lys,
        N, N-dimethyl-Lys or N, N, N-trimethyl-Lys; Xaa at
        residue 13 is Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr.
  <400> 186
  Xaa Asn Cys Cys Ser Ile Xaa Gly Cys Xaa Xaa Xaa Xaa Gly Asp Xaa
Cys Ser Xaa Val Arg
  <210> 187
  <211> 16
  <212> PRT
  <213> Conus catus
  <221> PEPTIDE
  <222> (6)..(13)
  <223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
        Xaa at residue 11 is Glu or gamma-carboxy-Glu.
  <400> 187
  Gly Cys Cys Ser Asn Xaa Val Cys His Leu Xaa His Xaa Asn Ala Cys
  <210> 188
  <211> 17
  <212> PRT
  <213> Conus catus
  <220>
  <221> PEPTIDE
  <222> (6)..(13)
  <223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
         Xaa at residue 9 is Tyr, nor-Tyr, mono-halo-Tyr,
         di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
         nitro-Tyr.
   <400> 188
   Gly Cys Cys Ser Asn Xaa Ile Cys Xaa Phe Asn Asn Xaa Arg Ile Cys
   Arg
   <210> 189
   <211> 17
   <212> PRT
   <213> Conus episcopatus
   <220>
   <221> PEPTIDE
   <222> (1)..(14)
   <223> Xaa at residues 1 and 14 is Glu or
         gamma-carboxy-Glu; Xaa at residues 6, 7 and 13 is
         Pro or hydroxy-Pro; Xaa at residue 10 is Tro (D or
         L) or halo-Trp.
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<220>

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<221> PEPTIDE
<222> (11)
<223> Xaa at residue 11 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 189
Xaa Cys Cys Ser Gln Xaa Xaa Cys Arg Xaa Xaa His Xaa Xaa Leu Cys
Ser
<210> 190
<211> 16
<21.2> PRT
<213> Conus geographus
<220>
<221> PEPTIDE
<222> (6)
<223> Xaa at residue 6 is Pro or hydroxy-Pro.
<400> 190
Gly Cys Cys Ser His Xaa Ala Cys Ala Gly Asn Asn Gln His Ile Cys
<210> 191
<211> 18
<212> PRT
<213> Conus geographus
<220>
<221> PEPTIDE
<222> (6), (13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
Gly Cys Cys Ala Val Xaa Ser Cys Arg Leu Arg Asn Xaa Asp Leu Cys
Gly Gly
<210> 192
<211> 16
 <212> PRT
<213> Conus imperialis
<220>
<221> NP BIND
<222> (6)..(13)
 <223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
 <400> 192
 Gly Cys Cys Ser His Xaa Ala Cys Asn Val Asn Asn Xaa His Ile Cys
 <210> 193
 <211> 20
 <212> PRT
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<213> Conus lividus
<220>
<221> PEPTIDE
<222> (2)..(10)
<223> Xaa at residues 2, 7, 9 and 10 is Pro or
      hydroxy-Pro; Xaa at residues 3 and 4 is Glu or
      gamma-carboxy-Glu.
<400> 193
Thr Xaa Xaa Xaa Cys Cys Xaa Asn Xaa Xaa Cys Phe Ala Thr Asn Ser
Asp Ile Cys Gly
<210> 194
<211> 17
<212> PRT
<213> Conus lividus
<220>
<221> PEPTIDE
<222> (7)..(12)
<223> Xaa at residue 7 is Pro or hydroxy-Pro; Xaa at
      residue 12 is Lys, N-methyl-Lys, N,N-dimethyl-Lys
      or N, N, N-trimethyl-Lys.
<400> 194
Asp Ala Cys Cys Ser Asp Xaa Arg Cys Ser Gly Xaa His Gln Asp Leu
Cys
<210> 195
<211> 17
<212> PRT
<213> Conus lividus
<220>
<221> PEPTIDE
<222> (1)..(7)
<223> Xaa at residue 1 is Glu or gamma-carboxy-Glu; Xaa
      at residue 7 is Pro or hydroxy-Pro.
<400> 195
Xaa Asp Cys Cys Ser Asp Xaa Arg Cys Ser Val Gly His Gln Asp Leu
Cys
<210> 196
<211> 16
<212> PRT
<213> Conus lividus
<220>
<221> PEPTIDE
<222> (6)
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<210> 200 <211> 21

75 <223> Xaa at residue 6 is Pro or hydroxy-Pro. <400> 196 Gly Cys Cys Ser His Xaa Ala Cys Ala Gly Ser Asn Ala His Ile Cys <210> 197 <211> 17 <212> PRT <213> Conus lividus <220> <221> PEPTIDE <222> (1)..(7) <223> Xaa at residue 1 is Glu or gamma-carboxy-Glu; Xaa at residue 7 is Pro or hydroxy-Pro. <400> 197 Xaa Asp Cys Cys Ser Asp Xaa Arg Cys Ser Val Gly His Gln Asp Met Cys <210> 198 <211> 16 <212> PRT <213> Conus lividus <220> <221> PEPTIDE <222> (6)..(13) <223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro. <400> 198 Gly Cys Cys Ser His Xaa Ala Cys Ala Gly Asn Asn Xaa His Ile Cys <210> 199 <211> 17 <212> PRT <213> Conus lividus <220> <221> PEPTIDE <222> (6)..(14) <223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro; Xaa at residue 14 is Tyr, mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or nitro-Tyr. <400> 199 Gly Cys Cys Gly Asn Xaa Ser Cys Ser Ile His Ile Xaa Xaa Val Cys Asn

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<212> PRT
<213> Conus lividus
<220>
<221> PEPTIDE
<222> (4)..(5)
<223> Xaa at residues 4 and 5 is Glu or
      gamma-carboxy-Glu.
<400> 200
Thr Asp Ser Xaa Xaa Cys Cys Leu Asp Ser Arg Cys Ala Gly Gln His
                                      10
Gln Asp Leu Cys Gly
<210> 201
<211> 17
<212> PRT
<213> Conus marmoreus
<220>
<221> PEPTIDE
<222> (6)..(15)
<223> Xaa at residues 6 and 7 is Pro or hydroxy-Pro; Xaa
      at residues 9 and 15 is Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 201
Gly Cys Cys Ser Asn Xaa Xaa Cys Xaa Ala Asn Asn Gln Ala Xaa Cys
Asn
<210> 202
<211> 16
<212> PRT
<213> Conus marmoreus
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 202
Gly Cys Cys Ser His Xaa Ala Cys Ser Val Asn Asn Xaa Asp Ile Cys
<210> 203
<211> 18
<212> PRT
<213> Conus musicus
<220>
<221> PEPTIDE
<222> (2)..(15)
<223> Xaa at residues 2 and 12 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys; Xaa at
       residue 14 is Pro or hydroxy-Pro.
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<221> PEPTIDE
<222> (16)
<223> Xaa at residue 16 is Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 203
Gly Xaa Cys Cys Ile Asn Asp Ala Cys Arg Ser Xaa His Xaa Gln Xaa
Cys Ser
<210> 204
<211> 17
<212> PRT
<213> Conus musicus
<220>
<221> PEPTIDE
<222> (4)..(15)
<223> Xaa at residues 4 and 15 is Tyr, nor-Tyr,
      mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,
      O-phospho-Tyr or nitro-Tyr; Xaa at residue 13 is
      Pro or hydroxy-Pro.
<400> 204
Gly Cys Cys Xaa Asn Ile Ala Cys Arg Ile Asn Asn Xaa Arg Xaa Cys
Arq
<210> 205
<211> 17
<212> PRT
<213> Conus obscurus
<221> PEPTIDE
<222> (6)..(15)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
      Xaa at residues 12 and 15 is Tyr, nor-Tyr,
      mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,
      O-phospho-Tyr or nitro-Tyr.
<220>
<221> PEPTIDE
<222> (14)
<223> Xaa at residue 14 is Lys, N-methyl-Lys,
       N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 205
Gly Cys Cys Ser His Xaa Val Cys Arg Phe Asn Xaa Xaa Xaa Xaa Cys
Gly
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<210> 206

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<211> 18
<212> PRT
<213> Conus obscurus
<221> PEPTIDE
<222> (2)..(15)
<223> Xaa at residue 2 is Glu or gamma-carboxy-Glu; Xaa
      at residues 7, 8 and 14 is Pro or hydroxy-Pro; Xaa
      at residue 15 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr
<400> 206
Asp Xaa Cys Cys Ala Ser Xaa Xaa Cys Arg Leu Asn Asn Xaa Xaa Val
Cys His
<210> 207
<211> 19
<212> PRT
<213> Conus obscurus
<220>
<221> PEPTIDE
<222> (6)..(18)
<223> Xaa at residue 6 is Pro or hydroxy-Pro; Xaa at
      residue 9 is Trp (D or L) or halo-Trp; Xaa at
      residues 14 and 18 is Glu or gamma-carboxy-Glu.
<220>
<221> PEPTIDE
<222> (15)
<223> Xaa at residue 15 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 207
Gly Cys Cys Ser Asn Xaa Val Cys Xaa Gln Asn Asn Ala Xaa Xaa Cys
Arg Xaa Ser
<210> 208
<211> 16
<212> PRT
<213> Conus obscurus
<220>
<221> PEPTIDE
<222> (6)..(15)
<223> Xaa at residues 6 and 7 is Pro or hydroxy-Pro; Xaa
      at residue 15 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 208
Gly Cys Cys Ser His Xaa Xaa Cys Ala Gln Asn Asn Gln Asp Xaa Cys
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<210> 209
 <211> 19
 <212> PRT
<213> Conus obscurus
 <220>
 <221> PEPTIDE
 <222> (6)..(15)
 <223> Xaa at residue 6 is Pro or hydroxy-Pro; Xaa at
       residues 14 and 18 is Glu or gamma-carboxy-Glu;
       Xaa at residue 15 is Tyr, nor-Tyr, mono-halo-Tyr,
       di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
       nitro-Tyr.
 <400> 209
 Gly Cys Cys Ser His Xaa Ala Cys Ser Gly Asn Asn Arg Xaa Xaa Cys
 Arg Xaa Ser
 <210> 210
 <211> 18
 <212> PRT
 <213> Conus omaria
 <220>
 <221> PEPTIDE
 <222> (2)..(15)
 <223> Xaa at residues 2, 7 and 14 is Pro or hydroxy-Pro;
       Xaa at residue 6 is Tyr, nor-Tyr, mono-halo-Tyr,
       di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
       nitro-Tyr; Xaa at residue 15 is Glu or
       gamma-carboxy-Glu
 <400> 210
 Asp Xaa Cys Cys Ser Xaa Xaa Asp Cys Gly Ala Asn His Xaa Xaa Ile
 Cys Gly
 <210> 211
 <211> 17
  <212> PRT
  <213> Conus omaria
 <221> PEPTIDE
 <222> (1)..(14)
  <223> Xaa at residues 1 and 14 is Glu or
        gamma-carboxy-Glu; Xaa at residues 6, 7 and 13 is
        Pro or hydroxy-Pro; Xaa at residue 10 is Trp (D or
        L) or halo-Trp.
  <220>
  <221> PEPTIDE
  <222> (11)
  <223> Xaa at resique 11 is Lys, N-methyl-Lys,
        N, N-damethyl-Lys or N, N, N-trimethyl-Lys.
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<400> 211
Xaa Cys Cys Ser Gln Xaa Xaa Cys Arg Xaa Xaa His Xaa Xaa Leu Cys
Ser
<210> 212
<211> 16
<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 212
Gly Cys Cys Ser His Xaa Ala Cys Ala Gly Asn Asn Xaa His Ile Cys
<210> 213
<211> 16
<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (6)..(15)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
      Xaa at residue 15 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 213
Gly Cys Cys Ser Asp Xaa Ser Cys Asn Val Asn Asn Xaa Asp Xaa Cys
<210> 214
<211> 18
<212> PRT
<213> Conus omaria
<220>
<221> PEPTIDE
<222> (1)..(7)
<223> Xaa at residues 1 and 2 is Glu or
      gamma-carboxy-Glu; Xaa at residue 7 is Pro or
      hydroxy-Pro.
<400> 214
Xaa Xaa Cys Cys Ser Asp Xaa Arg Cys Ser Val Gly His Gln Asp Met
Cys Arg
<210> 215
<211> 17
<212> PRT
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81
<213> Conus purpurascens
<220>
<221> PEPTIDE
<222> (7)..(15)
<223> Xaa at residue 7 is Pro or hydroxy-Pro; Xaa at
      residue 15 is Glu or gamma-carboxy-Glu.
<400> 215
Gly Gly Cys Cys Ser Asn Xaa Ala Cys Leu Val Asn His Leu Xaa Met
Cys
<210> 216
<211> 18
<212> PRT
<213> Conus purpurascens
<220>
<221> PEPTIDE
<222> (3)..(15)
<223> Xaa at residues 3, 8 and 15 is Pro or hydroxy-Pro.
<400> 216
Arg Asp Xaa Cys Cys Phe Asn Xaa Ala Cys Asn Val Asn Asn Xaa Gln
Ile Cys
<210> 217
<211> 21
<212> PRT
<213> Conus purpurascens
<220>
<221> PEPTIDE
<222> (5)..(8)
<223> Xaa at residue 5 is Pro or hydroxy-Pro; Xaa at
      residue 8 is Trp (D or L) or halo-Trp.
<400> 217
Cys Cys Ser Asp Xaa Ser Cys Xaa Arg Leu His Ser Leu Ala Cys Thr
Gly Ile Val Asn Arg
<210> 218
<211> 16
<212> PRT
<213> Conus purpurascens
<220>
<221> PEPTIDE
<223> Xaa at residue 5 is Pro or hydroxy-Pro.
<400> 218
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82
Cys Cys Thr Asn Xaa Ala Cys Leu Val Asn Asn Ile Arg Phe Cys Gly
<210> 219
<211> 18
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (2)..(7)
<223> Xaa at residue 2 is Glu or gamma-carboxy-Glu; Xaa
      at residue 7 is Pro or hydroxy-Pro.
<400> 219
Asp Xaa Cys Cys Ser Asp Xaa Arg Cys His Gly Asn Asn Arg Asp His
Cys Ala
<210> 220
<211> 17
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 220
Asp Cys Cys Ser His Xaa Leu Cys Arg Leu Phe Val Xaa Gly Leu Cys
Ile
<210> 221
<211> 17
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
      Xaa at residue 9 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<220>
<221> PEPTIDE
<222> (12)
<223> Xaa at residue 12 is Tyr, nor-Tyr, mono-halo-Tyr,
      di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
      nitro-Tyr.
<400> 221
Gly Cys Cys Ser His Xaa Val Cys Xaa Val Arg Xaa Xaa Asp Leu Cys
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Ara
<210> 222
<211> 16
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 222
Gly Cys Cys Ser His Xaa Ala Cys Asn Val Asn Asn Xaa His Ile Cys
                                      1.0
<210> 223
<211> 16
<212> PRT
<213> Conus regius
<220>
<221> PEPTIDE
<222> (6)..(12)
<223> Xaa at residue 6 is Pro or hydroxy-Pro; Xaa at
      residue 12 is Tyr, nor-Tyr, nor-Tyr,
      mono-halo-Tyr, di-halo-Tyr, O-sulpho-Tyr,
      O-phospho-Tyr or nitro-Tyr.
<220>
<221> PEPTIDE
<222> (9)
<223> Xaa at residue 9 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 223
Gly Cys Cys Ser His Xaa Val Cys Xaa Val Arg Xaa Ser Asp Met Cys
                                      1.0
<210> 224
<211> 17
<212> PRT
<213> Conus stercusmuscarum
<220>
<221> PEPTIDE
<222> (7)..(14)
 <223> Xaa at residues 7 and 14 is Pro or hydroxy-Pro;
       Xaa at residue 10 is Lys, N-methyl-Lys,
       N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
 <400> 224
 Gly Gly Cys Cys Ser His Xaa Ala Cys Xaa Val His Phe Xaa His Ser
 Cys
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<210> 225

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<211> 20
<212> PRT
<213> Conus stercusmuscarum
<220>
<221> PEPTIDE
<222> (6)..(14)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro;
      Xaa at residue 14 is Glu or gamma-carboxy-Glu.
<400> 225
Val Cys Cys Ser Asn Xaa Val Cys His Val Asp His Xaa Xaa Leu Cys
Arg Arg Arg Arg
<210> 226
<211> 17
<212> PRT
<213> Conus striatus
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 226
Gly Cys Cys Ser His Xaa Val Cys Asn Leu Ser Asn Xaa Gln Ile Cys
Arq
<210> 227
<211> 18
<212> PRT
<213> Conus textile
<220>
<221> PEPTIDE
<222> (1)..(15)
<223> Xaa at residue 1 is Gln or pyro-Glu; Xaa at
      residues 2 and 15 is Glu or gamma-carboxy-Glu; Xaa
      at residues 7 and 14 is Pro or hydroxy-Pro.
<400> 227
Xaa Xaa Cys Cys Ser His Xaa Ala Cys Asn Val Asp His Xaa Xaa Ile
Cys Arg
 <210> 228
 <211> 17
 <212> PRT
 <213> Conus tulipa
 <220>
 <221> PEPTIDE
 <222> (6)
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85
<223> Xaa at residue 6 is Pro or hydroxy-Pro.
<400> 228
Gly Cys Cys Ser Asn Xaa Ala Cys Leu Val Asn His Ile Arg Phe Cys
Gly
<210> 229
<212> PRT
<213> Conus virgo
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6 and 13 is Pro or hydroxy-Pro.
<400> 229
Asp Cys Cys Asp Asp Xaa Ala Cys Thr Val Asn Asn Xaa Gly Leu Cys
Thr
<210> 230
<211> 20
<212> PRT
<213> Conus textile
<220>
<221> PEPTIDE
<222> (6)..(13)
<223> Xaa at residues 6, 7 and 13 is Pro or hydroxy-Pro;
Xaa at residue 11 is Lys, N-methyl-Lys,
       N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 230
Gly Cys Cys Ser Asn Xaa Xaa Cys Ile Ala Xaa Asn Xaa His Met Cys
Gly Gly Arg Arg
<210> 231
<211> 18
 <212> PRT
 <213> Conus geographus
 <220>
 <221> PEPTIDE
 <222> (5)..(9)
 <223> Xaa at residue 5 is Pro or hydroxy-Pro; Xaa at
       residue 8 is Tyr, nor-Tyr, mono-halo-Tyr,
       di-halo-Tyr, O-sulpho-Tyr, O-phospho-Tyr or
nitro-Tyr; Xaa at residue 9 is Glu or
       gamma-carboxy-Glu.
 <220>
 <221> PEPTIDE
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<222> (10)..(14)
<223> Xaa at residues 10, 11, 12 and 14 is Lys,
      N-methyl-Lys, N,N-dimethyl-Lys or
      N, N, N-trimethyl-Lys.
<400> 231
Cys Cys Thr Ile Xaa Ser Cys Xaa Xaa Xaa Xaa Xaa Ile Xaa Ala Cys
Val Phe
<210> 232
<211> 18
<212> PRT
<213> Conus regius
<221> PEPTIDE
<222> (6)..(16)
<223> Xaa at residues 6 and 16 is Pro or hydroxy-Pro;
      Xaa at residue 13 is Lys, N-methyl-Lys,
      N, N-dimethyl-Lys or N, N, N-trimethyl-Lys.
<400> 232
Gly Cys Cys Gly Asn Xaa Ala Cys Ser Gly Ser Ser Xaa Asp Ala Xaa
Ser Cys
<210> 233
<211> 108
<212> DNA
<213> Conus imperialis
<220>
<221> CDS
<222> (1)..(105)
<400> 233
tot gat gga aag agt goo gog goo aaa goo aaa cog tot cac otg acg
Ser Ásp Gly Lys Ser Ála Ála Ála Lys Ála Lys Pro Ser His Leu Thr
got oca tto ato agg gao gaa tgo tgt too gat tot ogo tgt ggo aag
Ala Pro Phe Ile Arg Asp Glu Cys Cys Ser Asp Ser Arg Cys Gly Lys
                                                                    108
aac tgt ctt tga
Asn Cys Leu
<210> 234
<211> 35
<212> PRT
<213> Conus imperialis
 <400> 234
 Ser Asp Gly Lys Ser Ala Ala Ala Lys Ala Lys Pro Ser His Leu Thr
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Ala Pro Phe Ile Arg Asp Glu Cys Cys Ser Asp Ser Arg Cys Gly Lys
Asn Cys Leu
           35
<210> 235
<211> 108
<212> DNA
<213> Conus imperialis
<220>
<221> CDS
<222> (1)..(105)
<400> 235
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Phe Asp Gly Arg Asn Ala Pro Ala Asp Asp Lys Ala Ser Asp Leu Ile
get caa ate gte agg aga gea tge tgt tee gat egt ege tgt aga tgg
Ala Gln Ile Val Arg Arg Ala Cys Cys Ser Asp Arg Arg Cys Arg Trp
                                                                                108
agg tgt ggt tga
Arg Cys Gly
<210> 236
<211> 35
<212> PRT
<213> Conus imperialis
<400> 236
Phe Asp Gly Arg Asn Ala Pro Ala Asp Asp Lys Ala Ser Asp Leu Ile
Ala Gln Ile Val Arg Arg Ala Cys Cys Ser Asp Arg Arg Cys Arg Trp
Arg Cys Gly
<210> 237
<211> 145
 <212> DNA
 <213> Conus regius
 <220>
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 <400> 237
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Ser Asp Gly Arg Asn Ala Ala Ala Asp Ala Arg Ala Ser Pro Arg Ile
 get ett tte ete agg tte aca tge tgt agg aga ggt ace tgt tee cag
 Ala Leu Phe Leu Arg Phe Thr Cys Cys Arg Arg Gly Thr Cys Ser Gln 20 25 30
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145
cac tgt ggt tgaagacact gctgctccag gaccctctga accacgacgt
His Cys Gly
<210> 238
<211> 35
<212> PRT
<213> Conus regius
<400> 238
Ser Asp Gly Arg Asn Ala Ala Ala Asp Ala Arg Ala Ser Pro Arg Ile
Ala Leu Phe Leu Arg Phe Thr Cys Cys Arg Arg Gly Thr Cys Ser Gln \frac{20}{30}
His Cys Gly
<210> 239
<211> 145
<212> DNA
<213> Conus regius
<221> CDS
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<400> 239
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Ser Asn Gly Arg Asn Ala Ala Ala Asp Ala Lys Ala Ser Gln Arg Ile
get cea tte ete agg gae tat tge tgt agg aga eat gee tgt aeg ttg Ala Pro Phe Leu Arg Asp Tyr Cys Cys Arg Arg His Ala Cys Thr Leu \frac{25}{20}
                                                                            96
att tgt ggt tgaagacget getgeteeag gaccetetga accaegacgt
                                                                            145
att cyc Gly
Ile Cys Gly
<210> 240
<211> 35
<212> PRT
<213> Conus regius
<400> 240
 Ser Asn Gly Arg Asn Ala Ala Ala Asp Ala Lys Ala Ser Gln Arg Ile
Ala Pro Phe Leu Arg Asp Tyr Cys Cys Arg Arg His Ala Cys Thr Leu 20 25 30
Ile Cys Gly
 <210> 241
 <211> 145
 <212> DNA
 <213> Conus regius
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	89												
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<400> 241 tot aat gga Ser Asn Gly 1	agg aat Arg Asn 5	gee ge Ala Al	a gcc a Ala	gac Asp	gcc Ala 10	aaa Lys	gcg Ala	tct Ser	caa Gln	egg Arg 15	atc Ile	48	
gct cca ttc Ala Pro Phe	ctc agg Leu Arg 20	gac ta Asp Ty	t tgc r Cys	tgt Cys 25	agg Arg	aga Arg	cct Pro	ccc Pro	tgt Cys 30	acg Thr	ttg Leu	96	
att tgt ggt Ile Cys Gly 35	tgaagac	get get	getec	ag ga	accct	ctga	a aco	cacga	acgt			145	
<210> 242 <211> 35 <212> PRT <213> Conus	regius												
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Ala Pro Phe	Leu Arg 20	Asp Ty	r Cys	Cys 25	Arg	Arg	Pro	Pro	Cys 30	Thr	Leu		
Ile Cys Gly 35													
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gcc ata agg Ala Ile Arg	ggt tgc Gly Cys 20	tgt tc Cys Se	c gat r Asp	cct Pro 25	ege Arg	tgt Cys	aga Arg	tat Tyr	aga Arg 30	tgt Cys	cgt Arg	96	
tgaagacgct q	getgetee	ag gacc	ctctg	a ac	cacg	acgt						136	
<210> 244 <211> 32 <212> PRT <213> Conus	regius												
<400> 244 Ser Asn Lys 1	Arg Lys	Asn Al	a Ala	Met	Leu 10	Asp	Met	Ile	Ala	Gln 15	His		

Lys Cys Val

Ala Ile Arg Gly Cys Cys Ser Asp Pro Arg Cys Arg Tyr Arg Cys Arg <210> 245 <211> 145 <212> DNA <213> Conus regius <220> <221> CDS <222> (1)..(105) <400> 245 ttt aat gga agg agt gee gea gee gae caa aat geg eet gge etg ate Phe Asn Gly Arg Ser Ala Ala Ala Asp Gln Asn Ala Pro Gly Leu Ile get caa gtc gtc aga ggg tgc tgt tcc gat ccc cgc tgc gcc tgg Ala Gln Val Val Arg Gly Gly Cys Cys Ser Asp Pro Arg Cys Ala Trp aga tgt ggt tgaagacgtt getgeteeag gaeectetga accaegaegt aga LyL Arg Cys Gly 35 <210> 246 <211> 35 <212> PRT <213> Conus regius <400> 246 Phe Asn Gly Arg Ser Ala Ala Ala Asp Gln Asn Ala Pro Gly Leu Ile Ala Gln Val Val Arg Gly Gly Cys Cys Ser Asp Pro Arg Cys Ala Trp Arg Cys Gly <210> 247 <211> 145 <212> DNA <213> Conus regius <220> <221> CDS <222> (1)..(105) <400> 247 ttt gat gga agg aat gee gea gee gac gee aaa gtg att aac aeg gte Phe Asp Gly Arg Asn Ala Ala Ala Asp Ala Lys Val Ile Asn Thr Val get ega ate gee tgg gat ata tge tgt tee gaa eet gae tgt aac eat Ala Arg Ile Ala Trp Asp Ile Cys Cys Ser Glu Pro Asp Cys Asn His aaa tgt gtt tgaagacgct tctgctccag gaccctctga accacgacgt

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<210> 248
<211> 35
<212> PRT
<213> Conus regius
<400> 248
Phe Asp Gly Arg Asn Ala Ala Ala Asp Ala Lys Val Ile Asn Thr Val
Ala Arg Ile Ala Trp Asp Ile Cys Cys Ser Glu Pro Asp Cys Asn His 20 \\ 25 \\ 30
Lys Cys Val
<210> 249
<211> 136
<212> DNA
<213> Conus regius
<220>
<221> CDS
<222> (1)..(96)
<400> 249
tot aat aaa agg aag aat goo goa atg ott gac atg atc got caa cac
Ser Asn Lys Arg Lys Asn Ala Ala Met Leu Asp Met Ile Ala Gln His
ged ata agg ggt tgd tgt tod gat oot ogd tgt aaa dat dag tgt ggt
Ála Ile Arg Gly Cýs Cýs Ser Ásp Pro Arg Cýs Lys His Gln Cys Gly
                                                                     136
tgaagacgct gctgctccag gaccctctga accacgacgt
<210> 250
<211> 32
<212> PRT
<213> Conus regius
<400> 250
Ser Asn Lys Arg Lys Asn Ala Ala Met Leu Asp Met Ile Ala Gln His
Ala Ile Arg Gly Cys Cys Ser Asp Pro Arg Cys Lys His Gln Cys Gly
<210> 251
<211> 136
<212> DNA
<213> Conus musicus
<221> CDS
<222> (1)..(105)
<400> 251
atc aag aat aca goa goo ago aac aaa gog tot ago otg gtg got ott
Ile Lys Asn Thr Ala Ala Ser Asn Lys Ala Ser Ser Lea Val Ala Leu
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gtt gtc agg gga tgc tgt tac aat cct gtc tgc aag aaa tat tat tgt
Val Val Arg Gly Cys Cys Tyr Asn Pro Val Cys Lys Tyr Tyr Cys
                                                                         136
tgg aaa gge tgatgeteea ggaceetetg aaccaegaeg t
Trp Lys Gly
<210> 252
<211> 35
<212> PRT
<213> Conus musicus
<400> 252
Ile Lys Asn Thr Ala Ala Ser Asn Lys Ala Ser Ser Leu Val Ala Leu
Val Val Arg Gly Cys Cys Tyr Asn Pro Val Cys Lys Lys Tyr Tyr Cys
Trp Lys Gly
<210> 253
<211> 148
<212> DNA
<213> Conus purpurascens
<220>
<221> CDS
<222> (1)..(117)
<400> 253
tot gaa ggc agg aat got gaa gcc atc gac aac gcc tta gac cag agg
Ser Glu Gly Arg Asn Ala Glu Ala Ile Asp Asn Ala Leu Asp Gln Arg
gat cca aag cga cag gag ccg ggg tgc tgt agg cat cct gcc tgt ggg
Asp Pro Lys Arg Gln Glu Pro Gly Cys Cys Arg His Pro Ala Cys Gly
aaq aac aga tgt gga aga cgc tgatgctcca ggaccctctg aaccacgacg t
Lys Asn Arg Cys Gly Arg Arg
<210> 254
<211> 39
<212> PRT
<213> Conus purpurascens
<400> 254
Ser Glu Gly Arg Asn Ala Glu Ala Ile Asp Asn Ala Leu Asp Gln Arg
Asp Pro Lys Arg Gln Glu Pro Gly Cys Cys Arg His Pro Ala Cys Gly 20 \  \  \, 25
Lys Asn Arg Cys Gly Arg Arg
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<210> 255 <211> 156 <212> DNA <213> Conus	music	cus											
<220> <221> CDS <222> (1)	(102)												
<400> 255 tot gat ggc Ser Asp Gly 1	agg a Arg <i>B</i>	aat att Asn Ile 5	gca Ala	gtc Val	gac Asp	gac Asp 10	aga Arg	tgg Trp	tct Ser	ttc Phe	tat Tyr 15	acg Thr	4.8
ctc ttc cat Leu Phe His	gct a Ala 1 20	act tgo Thr Cys	tgt Cys	gcc Ala	gat Asp 25	cct Pro	gac Asp	tgt Cys	aga Arg	ttc Phe 30	cgg Arg	ccc Pro	96
ggt tgt tgat Gly Cys	ctttç	jt tott	caaa	ga co	getge	etgge	cca	aggad	cct	ctga	aacc	acg	15
acgt													15
<210> 256 <211> 34 <212> PRT <213> Conus <400> 256	music	cus											
Ser Asp Gly	Arg A	Asn Ile 5	e Ala	Val	Asp	Asp 10	Arg	Trp	Ser	Phe	Tyr 15	Thr	
Leu Phe His	Ala 1	Thr Cys	Cys	Ala	Asp 25	Pro	Asp	Cys	Arg	Phe 30	Arg	Pro	
Gly Cys													
<210> 257 <211> 142 <212> DNA <213> Conus	music	cus											
<220> <221> CDS <222> (1)	(102)												
<400> 257 atc aag aat Ile Lys Asn 1	act o	gca gce Ala Ala 5	c agc a Ser	aac Asn	aaa Lys	gcg Ala 10	cct Pro	agc Ser	ctg Leu	gtg Val	gct Ala 15	att Ile	41
gcc gtc agg Ala Val Arg	gga Gly 20	tgc tg Cys Cy:	t tac s Tyr	aat Asn	cct Pro 25	tcc Ser	tgt Cys	tgg Trp	ccg Pro	aaa Lys 30	aca Thr	tat Tyr	96

<210> 258 <211> 34

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<212> PRT
<213> Conus musicus
<400> 258
Ile Lys Asn Thr Ala Ala Ser Asn Lys Ala Pro Ser Leu Val Ala Ile
Ala Val Arg Gly Cys Cys Tyr Asn Pro Ser Cys Trp Pro Lys Thr Tyr \frac{20}{20}
Cys Ser
<211> 161
<212> DNA
<213> Conus musicus
<220>
<221> CDS
<222> (1)..(108)
<400> 259
tot gat age agg aat gtc goa atc gag gac aga gtg tot gac ctg cac
Ser Asp Ser Arg Asn Val Ala Ile Glu Asp Arg Val Ser Asp Leu His
tot atg tto tto gat gtt tot tgo tgt ago aat cot aco tgt aaa gaa
Ser Met Phe Phe Asp Val Ser Cys Cys Ser Asn Pro Thr Cys Lys Glu
acg tat ggt tgt tgatcgttgg ttttgaagac gctgatgctc caggaccctc
                                                                     148
Thr Tyr Gly Cys
                                                                     161
tgaaccacga cgt
<210> 260
<211> 36
<212> PRT
<213> Conus musicus
<400> 260
Ser Asp Ser Arg Asn Val Ala Ile Glu Asp Arg Val Ser Asp Leu His
Ser Met Phe Phe Asp Val Ser Cys Cys Ser Asn Pro Thr Cys Lys Glu
Thr Tyr Gly Cys
<210> 261
<211> 156
<212> DNA
<213> Conus musicus
<221> CDS
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ctc ttc cat Leu Phe His	get of Ala P	cat tgc His Cys	tgt Cys	gcc Ala	aat Asn 25	ccc Pro	atc Ile	tgt Cys	aaa Lys	aac Asn 30	acg Thr	ccc Pro	96
ggt tgt tg: Gly Cys	atcttt	gt tott	caaag	a co	getge	ctggd	c cca	aggad	ccct	ctga	aacca	ıcg	152
acgt													156
<210> 262 <211> 34 <212> PRT <213> Conus	s musio	cus											
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Leu Phe Hi	s Ala I 20	His Cys	Cys	Ala	Asn 25	Pro	Ile	Cys	Lys	Asn 30	Thr	Pro	
Gly Cys													
<210> 263 <211> 161 <212> DNA <213> Conu	s musi	cus											
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tot atg tt Ser Met Ph	c ttc e Phe 20	gat att Asp Ile	gct Ala	tgc Cys	tgt Cys 25	aac Asn	aat Asn	cct Pro	acc Thr	tgt Cys 30	aaa Lys	gaa Glu	96
acg tat gg Thr Tyr Gl 3	y Cys	tgategt	tgg t	:ttt	gaag	ac go	ctgai	gct	c ca	ggac	sete		148
tgaaccacga	cgt												161
<210> 264 <211> 36 <212> PRT <213> Conu	s musi	.cus											
<400> 264 Ser Asp Gl	y Arg	Asn Val	Ala	Ile	Asp	Asp 10	Arg	Val	Ser	Asp	Leu 15	His	

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Ser Met Phe Phe Asp Ile Ala Cys Cys Asn Asn Pro Thr Cys Lys Glu
Thr Tyr Gly Cys
<210> 265
<211> 161
<212> DNA
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<220>
<221> CDS
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Ser Ásp Gly Arg Asn Val Ála Ile Glú Ásp Arg Val Ser Ásp Leu Leu
tet atg ete tte gat gtt get tge tgt age aat eet gte tgt aaa gaa
Ser Met Leu Phe Asp Val Ala Cys Cys Ser Asn Pro Val Cys Lys Glu
acg tat ggt tgt tgatcgttgg ttttgaagac gctgatgete caggaccete
                                                                        148
Thr Tyr Gly Cys
                                                                        161
tqaaccacqa cgt
<210> 266
<211> 36
<212> PRT
<213> Conus musicus
<400> 266
Ser Asp Gly Arg Asn Val Ala Ile Glu Asp Arg Val Ser Asp Leu Leu
Ser Met Leu Phe Asp Val Ala Cys Cys Ser Asn Pro Val Cys Lys Glu
Thr Tyr Gly Cys
 <210> 267
 <211> 154
 <212> DNA
 <213> Conus betulinus
 <220>
 <221> CDS
 <222> (1)..(123)
 <400> 267
 tat gat ggc agg aat gct gcc gcc gac gac aaa gct ttt gac ctg ctg
 Tyr Asp Gly Arg Asn Ala Ala Ala Asp Asp Lys Ala Phe Asp Leu Leu
 get atg acc ata agg gga gga tgc tgt tcc tat cct ccc tgt atc gcg
 Ala Met Thr Ile Arg Gly Gly Cys Cys Ser Tyr Pro Pro Cys Ile Ala
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25 30 agt aat cet aaa tgt ggt gga aga ege tgatgeteea ggaecetetg Ser Asn Pro Lys Cys Gly Gly Arg Arg 143 154 aaccacaacg t <210> 268 <211> 41 <212> PRT <213> Conus betulinus <400> 268 Tyr Asp Gly Arg Asn Ala Ala Ala Asp Asp Lys Ala Phe Asp Leu Leu Ala Met Thr Ile Arg Gly Gly Cys Cys Ser Tyr Pro Pro Cys Ile Ala Ser Asn Pro Lys Cys Gly Gly Arg Arg 35 <210> 269 <211> 151 <212> DNA <213> Conus lividus <220> <221> CDS <222> (1)..(111) <400> 269 ttt gat ggc agg aat gct gca ggc aac gcc aaa atg tcc gcc ctg atg Phe Asp Gly Arg Asn Ala Ala Gly Asn Ala Lys Met Ser Ala Leu Met 1 gee etg ace ate agg gga tge tgt tee cat eet gte tgt age geg atg 96 Ala Leu Thr Ile Arg Gly Cys Cys Ser His Pro Val Cys Ser Ala Met agt cca atc tgt ggc tgaagacgct gatgccccag gaccctctga accacgacgt Ser Pro Ile Cys Gly 35 <210> 270 <211> 37 <212> PRT <213> Conus lividus <400> 270 Phe Asp Gly Arg Asn Ala Ala Gly Asn Ala Lys Met Ser Ala Leu Met Ala Leu Thr Ile Arg Gly Cys Cys Ser His Pro Val Cys Ser Ala Met Ser Pro Ile Cys Gly 35

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<210> 271
<211> 196
<212> DNA
<213> Conus musicus
<220>
<221> CDS
<222> (1)..(165)
<400> 271
atc aag aat get gea get gae gae aaa gea tet gae etg ete tet eag
Ile Lys Asn Ála Ála Ála Ásp Ásp Lys Ála Ser Ásp Leu Leu Ser Gln
ato gto agg aat got goa too aat gac aaa ggg tot gac otg atg act
Ile Val Arg Asn Ala Ala Ser Asn Asp Lys Gly Ser Asp Leu Met Thr
              20
ctt gcc ctc agg gga tgc tgt aaa aat cct tac tgt ggt gcg tcg aaa
                                                                     144
Leu Ala Leu Arg Gly Cys Cys Lys Asn Pro Tyr Cys Gly Ala Ser Lys
aca tat tgt ggt aga aga cgc tgatgctcca ggaccetetg aaccacgacg t
Thr Tyr Cys Gly Arg Arg Arg
<210> 272
<211> 55
<212> PRT
<213> Conus musicus
<400> 272
Ile Lys Asn Ala Ala Ala Asp Asp Lys Ala Ser Asp Leu Leu Ser Gln
Ile Val Arg Asn Ala Ala Ser Asn Asp Lys Gly Ser Asp Leu Met Thr 20 25 30
Leu Ala Leu Arg Gly Cys Cys Lys Asn Pro Tyr Cys Gly Ala Ser Lys
 Thr Tyr Cys Gly Arg Arg Arg
50 55
 <210> 273
 <211> 139
 <212> DNA
 <213> Conus omaria
 <220>
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 <222> (40)..(108)
 <400> 273
 totgatggca ggaatgccgc agcgtctgac ctgatggat ctg acc atc aag gga
Leu Thr Ile Lys Gly
 tgc tgt tct tat cct ccc tgt ttc gcg act aat cca gac tgt ggt cga
 Cys Cys Ser Tyr Pro Pro Cys Phe Ala Thr Asn Pro Asp Cys Gly Arg
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139 cga cgc tgatgctcca ggaccctctg aaccacgacg t Arg Arg <210> 274 <211> 23 <212> PRT <213> Conus omaria <400> 274 Leu Thr Ile Lys Gly Cys Cys Ser Tyr Pro Pro Cys Phe Ala Thr Asn Pro Asp Cys Gly Arg Arg Arg <210> 275 <211> 126 <212> DNA <213> Conus radiatus <220> <221> CDS <222> (1)..(123) <400> 275 ttt gat ggc agg aat gcc gca gcc gac tac aaa ggg tct gaa ttg ctc Phe Āsp Gly Arg Asn Āla Āla Āla Āsp Tyr Lys Gly Ser Glu Leu Leu got atg acc gtc agg gga gga tgc tgt tcc tat cct ccc tgt atc gca Ala Met Thr Val Arg Gly Gly Cys Cys Ser Tyr Pro Pro Cys Ile Ala 126 aat aat oot ott tgt got gga aga ogo tga Asn Asn Pro Leu Cys Ala Gly Arg Arg 35 <210> 276 <211> 41 <212> PRT <213> Conus radiatus <400> 276 Phe Asp Gly Arg Asn Ala Ala Ala Asp Tyr Lys Gly Ser Glu Leu Leu Ala Met Thr Val Arg Gly Gly Cys Cys Ser Tyr Pro Pro Cys Ile Ala Asn Asn Pro Leu Cys Ala Gly Arg Arg <210> 277 <211> 126 <212> DNA <213> Conus radiatus <220> <221> CDS <222> (1)..(123)

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gct atg acc Ala Met Thr														96
aat aat cct Asn Asn Pro 35							tga							126
<210> 278 <211> 41 <212> PRT <213> Conus	radi	atus												
<400> 278 Phe Asp Gly 1	Arg.	Asn 5	Ala	Ala	Ala	Asp	Tyr 10	Lys	Gly	Ser	Glu	Leu 15	Leu	
Ala Met Thr	Val	Arg	Gly	Gly	Cys	Cys 25	Ser	Tyr	Pro	Pro	Cys 30	Ile	Ala	
Asn Asn Pro 35	Phe	Cys	Ala	Gly	Arg 40	Arg								
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<220> <221> CDS <222> (1)	(114)													
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gct cag gcc Ala Gln Ala	atc Ile 20	ctt Leu	cga Arg	gat Asp	tgc Cys	tgt Cys 25	tcc Ser	aat Asn	cct Pro	ccc Pro	tgt Cys 30	tcc Ser	caa Gln	96
aat aat cca Asn Asn Pro 35				taa	agac	gct	gctt	gctc	ca g	gacc	ctct	g		144
aaccacgacg	t													155
<210> 280 <211> 38 <212> PRT <213> Conus	virg	10												
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101 Ala Gln Ala Ile Leu Arg Asp Cys Cys Ser Asn Pro Pro Cys Ser Gln Asn Asn Pro Asp Cys Met 35 <210> 281 <211> 155 <212> DNA <213> Conus virgo <221> CDS <222> (1)..(114) <400> 281 tot tat ggc agg tat gcc tca ccc gtc gac aga gcg tct gcc ctg atc Ser Tyr Gly Arg Tyr Ala Ser Pro Val Asp Arg Ala Ser Ala Leu Ile gct cag gcc atc ctt cga gat tgc tgc tgc aat cct cct tgt gcc cat Ala Gln Ala Ile Leu Arg Asp Cys Cys Ser Asn Pro Pro Cys Ala His 144 aat aat cca gac tgt cgt taaagacgct gettgeteea ggaceetetg Asn Asn Pro Asp Cys Arg aaccacgacg t <210> 282 <211> 38 <212> PRT <213> Conus virgo <400> 282 Ser Tyr Gly Arg Tyr Ala Ser Pro Val Asp Arg Ala Ser Ala Leu Ile Ala Gln Ala Ile Leu Arg Asp Cys Cys Ser Asn Pro Pro Cys Ala His Asn Asn Pro Asp Cys Arg 35 <210> 283 <211> 126 <212> DNA <213> Conus achatinus <220> <221> CDS <222> (1)..(123) <400> 283 tet gat ggc agg aat gee gea gee aac gae aaa geg tet ggc atg age Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Ala Ser Gly Met Ser

gcg ctg gcc gtc aat gaa tgc tgt acc aac cct gtc tgt cac gcg gaa Ala Leu Ala Val Asn Glu Cys Cys Thr Asn Pro Val Cys His Ala Glu

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<210> 284

<211> 41

<212> PRT <213> Conus achatinus

<400> 284

Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Ala Ser Gly Met Ser

Ala Leu Ala Val Asn Glu Cys Cys Thr Asn Pro Val Cys His Ala Glu

His Gln Glu Leu Cys Ala Arg Arg Arg

cat caa gaa ctt tgt gct aga aga cgc tga His Gln Glu Leu Cys Ala Arg Arg Arg

<210> 285 <211> 126

<212> DNA

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1

Pi.

T.

<213> Conus achatinus

<220> <221> CDS

<222> (1)..(123)

<400> 285

tot gat ggc agg aat gcc gca gcc aac gac aaa gcg tot gac gtg atc Ser Āsp Gly Arg Asn Āla Āla Āla Asn Āsp Lys Āla Ser Āsp Val Ile

acg etg gee etc aag gga tge tgt tec aac eet gte tgt cae ttg gag Thr Leu Ala Leu Lys Gly Cys Cys Ser Asn Pro Val Cys His Leu Glu

cat toa aac ott tgt ggt aga aga ogo tga His Ser Asn Leu Cys Gly Arg Arg Arg

126

<210> 286

<211> 41 <212> PRT

<213> Conus achatinus

<400> 286

Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Ala Ser Asp Val Ile

Thr Leu Ala Leu Lys Gly Cys Cys Ser Asn Pro Val Cys His Leu Glu

His Ser Asn Leu Cys Gly Arg Arg Arg

<210> 287

<211> 126

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<2123 <213			acha	tinu	s											
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gcg Ala	ctg ç Leu <i>I</i>	jcc Ala	gtc Val 20	aat Asn	gaa Glu	tgc Cys	tgt Cys	acc Thr 25	aac Asn	cct Pro	gtc Val	tgt Cys	cac His 30	gtg Val	gaa Glu	96
	caa q Gln (tga							126
<211 <212	> 288 > 41 > PR: > Cor	2	acha	atin	ıs											
<400 Ser 1	> 280 Asp (3 31y	Arg	Asn 5	Ala	Ala	Ala	Asn	Asp 10	Lys	Ala	Ser	Gly	Met 15	Ser	
Ala	Leu :	Ala	Val 20	Asn	Glu	Cys	Cys	Thr 25	Asn	Pro	Val	Cys	His 30	Val	Glu	
His	Gln	Glu 35	Leu	Cys	Ala	Arg	Arg 40	Arg								
<211 <212)> 28 .> 22 ?> DN 3> Co	0 A	amm	iral	is											
)> L> CD 2> (1		(180)												
ato)> 28 ttc Phe	acc	gtg Val	ttt Phe 5	Leu	ttg Leu	gtt Val	gtc Val	ttg Leu 10	gca Ala	acc Thr	acc Thr	gtc Val	gtt Val 15	Ser	48
ttc Phe	act Thr	tca Ser	gat Asp 20	Arg	gca Ala	ttt Phe	cgt Arg	ggc Gly 25	' Arg	aat Asn	gcc Ala	gca Ala	gcc Ala 30	. Lys	gcg Ala	96
tct Ser	ggc Gly	ctg Leu 35	Val	ggt Gly	ctç Lev	acc Thr	gac Asp 40	Lys	ago Aro	caa Glr	gaa Glu	tgc Cys 45	Cys	tet Ser	tat Tyr	144
cct Pro	gcc Ala 50	tgt Cys	aac Asr	cta Lev	gat Asp	cat His	Pro	gaa Glu	ı ctt	tgt Cys	ggt G1 <u>y</u> 60	,	agac	get		190
gati	getec	ag	gaco	ectet	:ga a	ecac	gaco	ŗt								220

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<210> 290
<211> 60
<212> PRT
<213> Conus ammiralis
<400> 290
Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser
Phe Thr Ser Asp Arg Ala Phe Arg Gly Arg Asn Ala Ala Ala Lys Ala
Ser Gly Leu Val Gly Leu Thr Asp Lys Arg Gln Glu Cys Cys Ser Tyr
Pro Ala Cys Asn Leu Asp His Pro Glu Leu Cys Gly
<210> 291
<211> 223
<212> DNA
<213> Conus ammiralis
<220>
<221> CDS
<222> (1)..(192)
<400> 291
atg ttc acc gtg ttt ctg ttg gtt gtc ttg gca acc act gtc gtt tcc
Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser
toc act toa ggt cgt cgt gca ttt cgt ggc agg aat gcc gca gcc aaa
Ser Thr Ser Gly Arg Arg Ala Phe Arg Gly Arg Asn Ala Ala Ala Lys
geg tet gga etg gte ggt etg act gac agg aga eca gaa tge tgt agt
                                                                       144
Ala Ser Gly Leu Val Gly Leu Thr Asp Arg Arg Pro Glu Cys Cys Ser
 gat cet ege tgt aac teg aet eat eea gaa ett tgt ggt gga aga ege
 Asp Pro Arg Cys Asn Ser Thr His Pro Glu Leu Cys Gly Gly Arg Arg
 tgatgeteca ggaceetetg aaccaegaeg t
 <210> 292
 <211> 64
 <212> PRT
 <213> Conus ammiralis
 <400> 292
 Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser
 Ser Thr Ser Gly Arg Arg Ala Phe Arg Gly Arg Asn Ala Ala Ala Lys
 Ala Ser Gly Leu Val Gly Leu Thr Asp Arg Arg Pro Glu Cys Cys Ser
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Asp Pro Arg Cys Asn Ser Thr His Pro Glu Leu Cys Gly Gly Arg Arg <210> 293 <211> 151 <212> DNA <213> Conus arenatus <220> <221> CDS <222> (1)..(120) <400> 293 tet gat gge agg aat gee gea gee aac geg tit gae etg ate gat etg Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Phe Asp Leu Ile Asp Leu ace gee agg cta aat tge tgt atg att eec eec tgt tgg aag aaa tat Thr Ala Arg Leu Asn Cys Cys Met Ile Pro Pro Cys Trp Lys Lys Tyr gga gac aga tgt agt gaa gta ege tgatgeteea ggaccetetg aaccaegaeg 150 Gly Asp Arg Cys Ser Glu Val Arg <210> 294 <211> 40 <212> PRT <213> Conus arenatus <400> 294 Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Phe Asp Leu Ile Asp Leu Thr Ala Arg Leu Asn Cys Cys Met Ile Pro Pro Cys Trp Lys Lys Tyr Gly Asp Arg Cys Ser Glu Val Arg <210> 295 <211> 126 <212> DNA <213> Conus arenatus <220> <221> CDS <222> (1)..(93) <400> 295 tet gat ggc agg aat gee gca ege aaa geg ttt gge tge tge gae tta Ser Asp Gly Arg Asn Ala Ala Arg Lys Ala Phe Gly Cys Cys Asp Leu ata occ tgt ttg gag aga tat ggt aac aga tgt aat gaa gtg cac Ile Pro Cys Leu Glu Arg Tyr Gly Asn Arg Cys Asn Glu Val His 93 25 126 tgatgeteca ggaccetetg aaccaegega egt

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<210> 296
<211> 31
<212> PRT
<213> Conus arenatus
<400> 296
Ser Asp Gly Arg Asn Ala Ala Arg Lys Ala Phe Gly Cys Cys Asp Leu
Ile Pro Cys Leu Glu Arg Tyr Gly Asn Arg Cys Asn Glu Val His
<210> 297
<211> 151
<212> DNA
<213> Conus arenatus
<220>
<221> CDS
<222> (1)..(120)
<400> 297
tet gat gge age aat gee gea gee aac gag tit gae etg ate get etg
Ser Ásp GÍy Ser Asn Ála Ála Ála Asn Glú Phe Ásp Leu Ile Ála Leu
acc gcc agg cta ggt tgc tgt aac gtt aca ccc tgt tgg gag aaa tat
Thr Ala Arg Leu Gly Cys Cys Asn Val Thr Pro Cys Trp Glu Lys Tyr
gga gac aaa tgt aat gaa gta cgc tgatgcttca ggaccctctg aaccacgacg
Gly Asp Lys Cys Asn Glu Val Arg
                                                                    151
<210> 298
<211> 40
<212> PRT
<213> Conus arenatus
<400> 298
Ser Asp Gly Ser Asn Ala Ala Ala Asn Glu Phe Asp Leu Ile Ala Leu
Thr Ala Arg Leu Gly Cys Cys Asn Val Thr Pro Cys Trp Glu Lys Tyr
Gly Asp Lys Cys Asn Glu Val Arg
<210> 299
<211> 148
<212> DNA
<213> Conus arenatus
<220>
<221> CDS
<222> (1)..(117)
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<400> 299 tot gat ggc agg aat gtc gca gca aaa gcg ttt cac cgg atc ggc cgg 48 Ser Asp Gly Arg Asn Val Ala Ala Lys Ala Phe His Arg Ile Gly Arg ace ate agg gat gaa tge tgt tee aat eet gee tgt agg gtg aat aat 96 Thr Ile Arg Asp Glu Cys Cys Ser Asn Pro Ala Cys Arg Val Asn Asn eca cae gtt tgt aga ega ege tgatgeteca ggaccetetg aaccaegaeg t Pro His Val Cys Arg Arg Arg <210> 300 <211> 39 <212> PRT <213> Conus arenatus <400> 300 Ser Asp Gly Arg Asn Val Ala Ala Lys Ala Phe His Arg Ile Gly Arg Thr Ile Arg Asp Glu Cys Cys Ser Asn Pro Ala Cys Arg Val Asn Asn Pro His Val Cys Arg Arg Arg <210> 301 <211> 151 <212> DNA <213> Conus arenatus <220> <221> CDS <222> (1)..(120) <400> 301 tet gat gge agg aat gee gea gee aac geg tit gae etg atg eet etg 48 Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Phe Asp Leu Met Pro Leu acc gec agg eta aat tge tgt age att eec gge tgt tgg aac gaa tat Thr Ala Arg Leu Asn Cys Cys Ser Ile Pro Gly Cys Trp Asn Glu Tyr 3.0 aaa gac aga tgt agt aaa gta cgc tgatgeteca ggaccetetg aaccacgacg Lys Asp Arg Cys Ser Lys Val Arg <210> 302 <211> 40 <212> PRT <213> Conus arenatus <400> 302 Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Phe Asp Leu Met Pro Leu

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Thr Ala Arg Leu Asn Cys Cys Ser Ile Pro Gly Cys Trp Asn Glu Tyr
Lys Asp Arg Cys Ser Lys Val Arg
<210> 303
<211> 157
<212> DNA
<213> Conus aurisiacus
<220>
<221> CDS
<222> (52)..(126)
<400> 303
tetqatggca ggaatgeege ageegaegae aaagegtetg acetggtege t etg gte
                                                          Leu Val
gtc agg gga gga tgc tgt tcc cac cct gtc tgt tac ttt aat aat cca
                                                                   105
Val Arg Gly Gly Cys Cys Ser His Pro Val Cys Tyr Phe Asn Asn Pro
caa atg tgt cgt gga aga cgc tgatgeteca ggaecetetg aaccacgacg t
Gln Met Cys Arg Gly Arg Arg
<210> 304
<211> 25
<212> PRT
<213> Conus aurisiacus
<400> 304
Leu Val Val Arg Gly Gly Cys Cys Ser His Pro Val Cys Tyr Phe Asn
Asn Pro Gln Met Cys Arg Gly Arg Arg
<210> 305
<211> 157
<212> DNA
<213> Conus aurisiacus
<220>
<221> CDS
<222> (52)..(126)
<400> 305
tetgatggca ggaatgeege ageegaegae aaagegtetg acetggtege t etg gee
                                                          Leu Ala
qtc aqq qga qqa tgc tgt tcc cac cct gtc tgt aac ttg aat aat cca
Val Arg Gly Gly Cys Cys Ser His Pro Val Cys Asn Leu Asn Asn Pro
caa atg tgt cgt gga aga cgc tgatgctcca ggaccctctg aaccacgacg t
Gln Met Cys Arg Gly Arg Arg
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<210> 306
<211> 25
<212> PRT
<213> Conus aurisiacus
<400> 306
Leu Ala Val Arg Gly Gly Cys Cys Ser His Pro Val Cys Asn Leu Asn
                                       10
Asn Pro Gln Met Cys Arg Gly Arg Arg
<210> 307
<211> 157
<212> DNA
<213> Conus betulinus
<220>
<221> CDS
<222> (1)..(117)
<400> 307
ttt cgt ggc agg aat coc gca gcc aac gac aaa agg tct gac ctg gcc
Phe Arg Gly Arg Asn Pro Ala Ala Asn Asp Lys Arg Ser Asp Leu Ala
get etg age gte agg gga gga tge tgt tee eat eet gee tgt age gtg Ala Leu Ser Val Arg Gly Gly Cys Cys Ser His Pro Ala Cys Ser Val
act cat cca gag ctt tgt ggc tgaagacgot gatgccccag gaccctctga
                                                                         147
Thr His Pro Glu Leu Cys Gly
                                                                         157
accacgacgt
<210> 308
<211> 39
<212> PRT
<213> Conus betulinus
<400> 308
Phe Arg Gly Arg Asn Pro Ala Ala Asn Asp Lys Arg Ser Asp Leu Ala
Ala Leu Ser Val Arg Gly Gly Cys Cys Ser His Pro Ala Cys Ser Val
Thr His Pro Glu Leu Cys Gly
          35
<210> 309
<211> 151
<212> DNA
<213> Conus betulinus
<221> CDS
<222> (1)..(120)
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<400> 309
tot gat ggc ggg aat gcc gca gcc aaa gcg tot gac ctg atc gct cag
Ser Asp Gly Gly Asn Ala Ala Ala Lys Ala Ser Asp Leu Ile Ala Gln
acc atc agg gga gga tgc tgt tcc tat cct gcc tgt agc gtg gaa cat
                                                                    96
Thr Ile Arg Gly Gly Cys Cys Ser Tyr Pro Ala Cys Ser Val Glu His
caa gac ctt tgt gat gga aga ege tgatgeteca ggaccetetg aaccaegaeg
Gln Asp Leu Cys Asp Gly Arg Arg
t
<210> 310
<211> 40
<212> PRT
<213> Conus betulinus
<400> 310
Ser Asp Gly Gly Asn Ala Ala Ala Lys Ala Ser Asp Leu Ile Ala Gln
Thr Ile Arg Gly Gly Cys Cys Ser Tyr Pro Ala Cys Ser Val Glu His \frac{20}{20}
Gln Asp Leu Cys Asp Gly Arg Arg
<210> 311
<211> 114
<212> DNA
<213> Conus caracteristicus
<220>
<221> CDS
<222> (1)..(111)
<400> 311
tot tat ggc agg aat goc goa goc aaa gog ttt gaa gtg agt tgc tgt
Ser Tyr Gly Arg Asn Ala Ala Ala Lys Ala Phe Glu Val Ser Cys Cys
gtc gtt cgc ccc tgt tgg att cgc tat caa gag gaa tgt ctt gaa gca
Val Val Arg Pro Cýs Trp Ile Arg Tyr Gln Glu Glu Cýs Leu Glu Ala
20 25 30
                                                                     114
gat cee agg ace etc tga
Asp Pro Arg Thr Leu
<210> 312
<211> 37
<212> PRT
<213> Conus caracteristicus
<400> 312
Ser Tyr Gly Arg Asn Ala Ala Ala Lys Ala Phe Glu Val Ser Cys Cys
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Val Val Arg Pro Cys Trp Ile Arg Tyr Gln Glu Glu Cys Leu Glu Ala
Asp Pro Arg Thr Leu
<210> 313
<211> 123
<212> DNA
<213> Conus caracteristicus
<220>
<221> CDS
<222> (1)..(120)
<400> 313
tot gat ggc agg aat gec gea gec aac gee ett gac etg ate aet etg
Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Leu Asp Leu Ile Thr Leu
atc qcc agg caa aat tgc tgt agc att ccc ggc tgt tgg gag aaa tat
Ile Ala Arg Gln Asn Cys Cys Ser Ile Pro Gly Cys Trp Glu Lys Tyr
                                                                   123
gga gac aaa tgt agt gaa gta cgc tga
Gly Asp Lys Cys Ser Glu Val Arg
<210> 314
<211> 40
<212> PRT
<213> Conus caracteristicus
<400> 314
Ser Asp Gly Arg Asn Ala Ala Ala Asn Ala Leu Asp Leu Ile Thr Leu
Ile Ala Arg Gln Asn Cys Cys Ser Ile Pro Gly Cys Trp Glu Lys Tyr
Gly Asp Lys Cys Ser Glu Val Arg
<210> 315
<211> 154
<212> DNA
<213> Conus catus
<220>
<221> CDS
<222> (1)..(123)
<400> 315
 tet gat ggc agg aat gaa gee gee aac gae gaa geg tet gae gtg atc
 Ser Asp Gly Arg Asn Glu Ala Ala Asn Asp Glu Ala Ser Asp Val Ile
 gag etg gee ete aag gga tge tgt tee aac eet gte tgt cae ttg gag
 Glu Leu Ala Leu Lys Gly Cys Cys Ser Asn Pro Val Cys His Leu Glu
                                  25
              20
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112	
cat oca aac got tgt ggt aga aga ogo tgatgotoca ggaccototg His Pro Asn Ala Cys Gly Arg Arg Arg 35	143
aaccacgacg t	154
<210> 316 <211> 41 <212> PRT <213> Conus catus	
$<\!400\!>$ 316 Ser Asp Gly Arg Asn Glu Ala Ala Asn Asp Glu Ala Ser Asp Val Ile $\frac{1}{1}$	
Glu Leu Ala Leu Lys Gly Cys Cys Ser Asn Pro Val Cys His Leu Glu $20 \hspace{1cm} 25 \hspace{1cm} 30 \hspace{1cm}$	
His Pro Asn Ala Cys Gly Arg Arg Arg 35	
<210> 317 <211> 154 <212> DNA <213> Conus catus	
<220> <221> CDS <222> (1)(123)	
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gct ctg gcc gtc agg gga tgc tgt tcc aac cct atc tgt tac ttt aat Ala Leu Ala Val Arg Gly Cys Cys Ser Asn Pro 11e Cys Tyr Phe Asn 20 25 30	96
aat cca cga att tgt cgt gga aga cgc tgatgeteca ggaccetetg Asn Pro Arg Ile Cys Arg Gly Arg Arg $$35\ $	143
aaccacgacg t	154
<210> 318 <211> 41 <212> PRT <213> Conus catus	
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Ala Leu Ala Val Arg Gly Cys Cys Ser Asn Pro Ile Cys Tyr Phe Asn $20 \hspace{0.2in} 25 \hspace{0.2in} 30$	
Asn Pro Arg Ile Cys Arg Gly Arg Arg 35 40	

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<210> 319
<211> 111
<212> DNA
<213> Conus episcopatus
<220>
<221> CDS
<222> (1)..(108)
<400> 319
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Ser His Gly Arg Asn Ala Ala Arg Lys Ala Ser Asp Leu Ile Ala Leu
acc gtc agg gaa tgc tgt tct cag cct ccc tgt cgc tgg aaa cat cca
Thr Val Arg Glu Cys Cys Ser Gln Pro Pro Cys Arg Trp Lys His Pro
                                                                        111
gaa ctt tgt agt tga
Glu Leu Cys Ser
<210> 320
<211> 36
<212> PRT
<213> Conus episcopatus
<400> 320
Ser His Gly Arg Asn Ala Ala Arg Lys Ala Ser Asp Leu Ile Ala Leu
Thr Val Arg Glu Cys Cys Ser Gln Pro Pro Cys Arg Trp Lys His Pro
Glu Leu Cys Ser
35
<210> 321
<211> 151
<212> DNA
<213> Conus geographus
<220>
<221> CDS
<222> (1)..(120)
<400> 321
tct gat ggc agg aat gac gca gcc aaa gcg ttt gac ctg ata tct tcg
Ser Asp Gly Arg Asn Asp Ala Ala Lys Ala Phe Asp Leu Ile Ser Ser
 ace gtc aag aaa gga tgc tgt tee eat eet gee tgt geg ggg aat aat
 Thr Val Lys Lys Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn Asn
 caa cat att tgt ggc cga aga cgc tgatgctcca ggaccctctg aaccacgacg
 Gln His Ile Cys Gly Arg Arg Arg
          35
 t
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<210> 322
<211> 40
<212> PRT
<213> Conus geographus
<400> 322
Ser Asp Gly Arg Asn Asp Ala Ala Lys Ala Phe Asp Leu Ile Ser Ser
Thr Val Lys Lys Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn Asn
Gln His Ile Cys Gly Arg Arg Arg
<210> 323
<211> 154
<212> DNA
<213> Conus geographus
<220>
<221> CDS
<222> (1)..(123)
<400> 323
tot gat ggc agg aat gcc gca gcc aac gac caa gcg tot gac ctg atg
Ser Āsp Gly Arg Asn Āla Āla Āla Asn Āsp Gln Āla Ser Āsp Leu Met
get geg acc gtc agg gga tgc tgt gcc gtt cet tec tgt cgc etc egt
Ala Ala Thr Val Arg Gly Cys Cys Ala Val Pro Ser Cys Arg Leu Arg
aat cca gac ctt tgt ggt gga gga cgc tgatgeteca ggaccetetg
                                                                   143
Asn Pro Asp Leu Cýs Gly Gly Arg
                                                                   154
aaccacgacg t
<210> 324
<211> 41
<212> PRT
<213> Conus geographus
<400> 324
Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Gln Ala Ser Asp Leu Met
Ala Ala Thr Val Arg Gly Cys Cys Ala Val Pro Ser Cys Arg Leu Arg
Asn Pro Asp Leu Cys Gly Gly Arg
<210> 325
<211> 120
 <212> DNA
 <213> Conus imperialis
<220>
 <221> CDS
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Glu Glu Cys Cys Pro Asn Pro Pro Cys Phe Ala Thr Asn Ser Asp Ile
Cys Gly Gly Arg Arg
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<220>
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Ser Asn Gly Arg Asn Ala Ala Ala Lys Phe Lys Ala Pro Ala Leu Met
aag egg ace gte agg gat get tge tgt tea gae eet ege tgt tee ggg Lys Arg Thr Val Arg Asp Ala Cys Cys Ser Asp Pro Arg Cys Ser Gly 20 25 30
                                                                        147
aaa cat caa gac ctg tgt ggc tgaagacgct gatgctccag gaccctctga
Lys His Gln Asp Leu Cys Gly
                                                                        157
accacgacgt
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 Ser Asn Gly Arg Asn Ala Ala Ala Lys Phe Lys Ala Pro Ala Leu Met
 Lys Arg Thr Val Arg Asp Ala Cys Cys Ser Asp Pro Arg Cys Ser Gly
 Lys His Gln Asp Leu Cys Gly
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 Ser Asn Gly Arg Asn Ala Ala Ala Lys Phe Lys Ala Pro Ala Leu Met
 gag ctg acc gtc agg gaa gat tgc tgt tca gac cct cgc tgt tcc gtg
 Glu Leu Thr Val Arg Glu Asp Cys Cys Ser Asp Pro Arg Cys Ser Val
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gga Gly	cat His	caa Gln 35	gac Asp	ctg Leu	tgt Cys	ggc Gly	tgaa	gacg	ct g	atgo	tcca	g ga	ccct	.ct.ga		147
acca	cgac	gt														157
<210 <211 <212 <213	> 39 > PR	T	livi	idus												
<400 Ser 1	> 33 Asn	2 Gly	Arg	Asn 5	Ala	Ala	Ala	Lys	Phe 10	Lys	Ala	Pro	Ala	Leu 15	Met	
Glu	Leu	Thr	Val 20	Arg	Glu	Asp	Суз	Cys 25	Ser	Asp	Pro	Arg	Cys 30	Ser	Val	
Gly	His	Gln 35	Asp	Leu	Cys	Gly										
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	.> C!		(126)												
оса)> 3: ttt Phe	gat	ggc Gly	agg Arg 5	aat Asn	gct Ala	gca Ala	gcc Ala	agc Ser 10	gac Asp	aaa Lys	gcg Ala	tcc Ser	gag Glu 15	ctg Leu	48
atg Met	gct Ala	ctg Leu	gcc Ala 20	Val	agg Arg	gga Gly	tgc Cys	tgt Cys 25	tcc Ser	cat His	cct Pro	gcc Ala	tgt Cys 30	Ala	ggg Gly	96
agt Ser	aat Asn	gca Ala 35	His	atc Ile	tgt Cys	ggc	aga Arg 40	Arg	ege Arg	tga	tgct	cca	ggac	cctc	tg	14
aac	cacg	acg	t													15
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Met Ala Leu Ala Val Arg Gly Cys Cys Ser His Pro Ala Cys Ala Gly $20 \hspace{0.2in} 25 \hspace{0.2in} 30 \hspace{0.2in}$

Ser Asn Ala His Ile Cys Gly Arg Arg Arg 35

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30

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aag ctg acc gtc agg gag gat tgc tgt tca gac cct cgc tgt tcc gtg Lys Leu Thr Val Arg Glu Asp Cys Cys Ser Asp Pro Arg Cys Ser Val \begin{array}{c} 25 \\ 20 \end{array}
gga cat caa gac atg tgt ggc tgaagacgct gatgctccag gaccctctga
                                                                          147
Gly His Gln Asp Met Cys Gly
          35
atcacgacgt
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Ser Asn Gly Arg Asn Ala Ala Ala Lys Phe Lys Ala Pro Ala Leu Met
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Gly His Gln Asp Met Cys Gly
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 Phe Glu Cys Arg Asn Ala Ala Gly Asn Asp Lys Ala Thr Asp Leu Met
 get etg act gte agg gga tge tgt tee eat eet gee tgt get ggg aat
 Ala Leu Thr Val Arg Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn
 aat cca cat atc tgc ggc tgaagacgct gatgctccag gaccctctga
                                                                          144
 Asn Pro His Ile Cys Gly
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accacgacgt														154
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Ala Leu Thr	Val 20	Arg	Gly	Cys	Cys	Ser 25	His	Pro	Ala	Cys	Ala 30	Gly	Asn	
Asn Pro His		Cys	Gly											
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<220> <221> CDS <222> (1)	(114	}												
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gct ctg act Ala Leu Thi														96
att cct tac Ile Pro Tym	. Val				agac	act (gatgo	etee	ag g	acce	tetg	a		144
accacgacgt														154
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Ala Leu Th	val 20		Gly	Cys	Суз	Gly 25	Asn	Pro	Ser	Cys	Ser 30	Ile	His	
Ile Pro Ty:		Cys	Asn											
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<213> Conus marmoreus

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Asn Gln Ala Tyr Cys Asn Gly Arg Arg
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<212> DNA
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Ser Asp Gly Arg Asn Ala Ala Ala Lys Asp Lys Ala Ser Asp Leu Val
get etg ace gte aag gga tge tgt tet eat eet gee tgt age gtg aat
                                                                   96
Ala Leu Thr Val Lys Gly Cys Cys Ser His Pro Ala Cys Ser Val Asn
aat cca gac att tgt ggt tga
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Asn Pro Asp Ile Cys Gly
         3.5
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Ser Asp Gly Arg Asn Ala Ala Ala Lys Asp Lys Ala Ser Asp Leu Val
Ala Leu Thr Val Lys Gly Cys Cys Ser His Pro Ala Cys Ser Val Asn
Asn Pro Asp Ile Cys Gly
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<212> DNA
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<220>
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Ser Asp Gly Arg Asn Ala Ala Ala Asn Asn Lys Val Ala Leu Thr Met
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agg gga aaa tgc tgt atc aat gat gcg tgt cgc tcg aaa cat cca cag Arg Gly Lys Cys Cys Ile Asn Asp Ala Cys Arg Ser Lys His Pro Gln tac tgt tet gga aga ege tgatacteca ggaccetetg aaccaegaeg t 145 Tyr Cys Ser Gly Arg Arg <210> 348 <211> 38 <212> PRT <213> Conus musicus <400> 348 Ser Asp Gly Arg Asn Ala Ala Ala Asn Asn Lys Val Ala Leu Thr Met Arg Gly Lys Cys Cys Ile Asn Asp Ala Cys Arg Ser Lys His Pro Gln Tyr Cys Ser Gly Arg Arg 35 <210> 349 <211> 154 <212> DNA <213> Conus musicus <220> <221> CDS <222> (1)..(123) <400> 349 tot gat ggc agg aat gct gca gcc aac gac aaa gtg tot gac cag atg Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Val Ser Asp Gln Met get etg gtt gtc agg gga tgc tgt tac aat att gcc tgt aga att aat Ála Leu Val Val Arg Gly Cys Cys Tyr Asn Ile Ála Cys Arg Ile Asn aat cca cgg tac tgt cgt gga aaa cgc tgatgttcca ggaccctctg 143 Asn Pro Arg Tyr Cys Arg Gly Lys Arg aaccacgacg t 154 <210> 350 <211> 41 <212> PRT <213> Conus musicus <400> 350 Ser Asp Gly Arg Asn Ala Ala Ala Asn Asp Lys Val Ser Asp Gln Met Ala Leu Val Val Arg Gly Cys Cys Tyr Asn Ile Ala Cys Arg Ile Asn Asn Pro Arg Tyr Cys Arg Gly Lys Arg

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gtc agg gga tgc tgt tcc cat cct gtc tgt cgc ttc aat tat cca aaa
Val Arg Gly Cys Cys Ser His Pro Val Cys Arg Phe Asn Tyr Pro Lys
tat tgt ggt gga aga cgc tgatggtcca ggaccctctg aaccacgacg t
Tyr Cys Gly Gly Arg Arg
<210> 352
<211> 24
<212> PRT
<213> Conus obscurus
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Leu Asn Val Arg Gly Cys Cys Ser His Pro Val Cys Arg Phe Asn Tyr
Pro Lys Tyr Cys Gly Gly Arg Arg
<210> 353
<211> 151
<212> DNA
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                                                   Leu Ala Leu Arg
gat gaa tgc tgt gcc agt cct ccc tgt cgt ttg aat aat cca tac gta
Asp Glu Cys Cys Ala Ser Pro Pro Cys Arg Leu Asn Asn Pro Tyr Val
                                                                   151
tgt cat tgacgacget gatgetecag gaccetetga accacgacgt
Cys His
<210> 354
<211> 22
<212> PRT
<213> Conus obscurus
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Leu Ala Leu Arg Asp Glu Cys Cys Ala Ser Pro Pro Cys Arg Leu Asn
Asn Pro Tyr Val Cys His
             20
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Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser
occ act toa gat ogt goa tot gat agg agg aat goo goa goo aaa gog
Pro Thr Ser Asp Arg Ala Ser Asp Arg Arg Asn Ala Ala Ala Lys Ala
ttt gac ctg aga tat tcg acc gcc aag aga gga tgc tgt tcc aat cct
                                                                   144
Phe Asp Leu Arg Tyr Ser Thr Ala Lys Arg Gly Cys Cys Ser Asn Pro
                                                                   186
gte tgt tgg cag aat aat gca gaa tac tgt cgt gaa agt ggc
Val Cys Trp Gln Asn Asn Ala Glu Tyr Cys Arg Glu Ser Gly
                                                                   217
taatgeteea ggaceetetg aaccacgacg t
<210> 356
<211> 62
<212> PRT
<213> Conus obscurus
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Met Phe Thr Val Phe Leu Leu Val Val Leu Ala Thr Thr Val Val Ser
Pro Thr Ser Asp Arg Ala Ser Asp Arg Arg Asn Ala Ala Lys Ala
Phe Asp Leu Arg Tyr Ser Thr Ala Lys Arg Gly Cys Cys Ser Asn Pro
         35
 Val Cys Trp Gln Asn Asn Ala Glu Tyr Cys Arg Glu Ser Gly
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 <212> DNA
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++0	act Thr	tca Ser	gat Asp 20	cat	gca Ala	tct Ser	gat Asp	ggc Gly 25	aaa	aat Asn	gtc Val	gca Ala	gcg Ala 30	tct	cac His	96
ctg Leu	atc Ile	gct Ala 35	ctg Leu	acc Thr	atc Ile	aag Lys	gga Gly 40	tgc Cys	tgt Cys	tct Ser	cac His	cct Pro 45	ccc Pro	tgt Cys	gcc Ala	144
cag Gln	aat Asn 50	aat Asn	caa Gln	gac Asp	tat Tyr	tgt Cys 55	ggt Gly	tga	egacç	get (gatgo	tcca	g ga	accct	ctga	198
acca	acga	egt														208
<21: <21: <21:		6 RT onus	obs	curu	S											
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Phe	Thr	Ser	Asp 20		Ala	Ser	Asp	Gly 25	Gly	Asn	Val	Ala	Ala 30	Ser	His	
Leu	Ile	Ala 35	Leu	Thr	Ile	Lys	Gly 40	Cys	Суз	Ser	His	Pro 45	Pro	Cys	Ala	
Gln	Asn 50		Glr	Asp	Tyr	Cys 55	Gly									
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tc: Se:	act Thi	to: Sei	a gat c Asp 2	o Aro	g gca	a tct a Ser	gat Asp	age Are	g Arq	g aat g Asi	gee Ala	gca Ala	gcc Ala 30	з груз	a gcg s Ala	96
tc1 Se	ga Ası	c ct	u Me	g tai	t too	g acc r Thi	gto Val	г та	g aaa s Ly:	a gg: s Gl:	a tgt y Cys	tgt Cys 45	ae:	c cat	cct Pro	144
gc Al	c tgr a Cy:	s Se	g gg r Gl	g aa y As:	t aa n As:	t oga n Aro	à em	a ta u Ty:	t tg r Cy.	t cg s Ar	t gaa g Glu	1 261	gg G1	= Y		186

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cet cet tgt ege tgg aaa cat eea gaa ett tgt agt tgaagaeget
                                                                      98
Pro Pro Cys Arg Trp Lys His Pro Glu Leu Cys Ser
gatgetecag gaccetetga accaegacgt
                                                                      128
<210> 364
<211> 21
<212> PRT
<213> Conus omaria
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Leu Thr Val Arg Glu Cys Cys Ser Gln Pro Pro Cys Arg Trp Lys His
Pro Glu Leu Cys Ser
<210> 365
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                                                             Leu Ala
gtc agg gga tgc tgt tcc cat cct gcc tgt gct ggg aat aat cca cat
Val Arg Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn Asn Pro His
ate tgt ggc aga aga cgc tgatgeteca ggaccetetg aaccacgacg t
Ile Cys Gly Arg Arg Arg
<210> 366
<211> 24
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Leu Ala Val Arg Gly Cys Cys Ser His Pro Ala Cys Ala Gly Asn Asn
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Pro His Ile Cys Gly Arg Arg Arg
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                                            Leu Thr Ile Lys Gly
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Cys Cys Ser Asp Pro Ser Cys Asn Val Asn Asn Pro Asp Tyr Cys Gly
                                                                   142
tgacgacget gatgetecag gaccetetga accaegacgt
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<211> 21
<212> PRT
<213> Conus omaria
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Leu Thr Ile Lys Gly Cys Cys Ser Asp Pro Ser Cys Asn Val Asn Asn
Pro Asp Tyr Cys Gly
<210> 369
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gtc agg gaa gaa tgc tgt tca gac cct cgc tgt tcc gtg gga cat caa
Val Arg Glu Glu Cys Cys Ser Asp Pro Arg Cys Ser Val Gly His Gln
gat atg tgt cgg tgaagcacgt gatgetecag gaccetetga accaegacgt
Asp Met Cys Arg
     20
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Leu Thr Val Arg Glu Glu Cys Cys Ser Asp Pro Arg Cys Ser Val Gly
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151

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         Thr Asp Gly Arg Asn Ala Ala Ala Ile Ala Leu Asp Leu Ile Ala Pro
         gee gtc agg gga gga tgc tgt tee aat eet gee tgt tta gtg aat eat
         Ála Val Arg Gly Gly Cys Cys Ser Asn Pro Ála Cys Leu Val Asn His
         cta gaa atg tgt ggt aaa aga cgc tgatgcccca ggaccetetg aaccacgaeg
         Leu Glu Met Cys Gly Lys Arg Arg
1
                  35
         t
1
         <210> 372
Fi.
         <211> 40
         <213> Conus purpurascens
         <400> 372
         Thr Asp Gly Arg Asn Ala Ala Ala Ile Ala Leu Asp Leu Ile Ala Pro
         Ala Val Arg Gly Gly Cys Cys Ser Asn Pro Ala Cys Leu Val Asn His
         Leu Glu Met Cys Gly Lys Arg Arg
         <210> 373
         <211> 160
         <212> DNA
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His Gln Asp Met Cys Arg

<213> Conus purpurascens

<210> 371 <211> 151 <212> DNA

<220>

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tgt ggt gga aga cgc tgatgcccca ggaccctctg aaccacgacg t $$\operatorname{Gly}$$ Arg Arg $$\operatorname{35}$$	142
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Thr Val Cys Cys Thr Asn Pro Ala Cys Leu Val Asn Asn Ile Arg Phe $20 \\ 25 \\ 30$	
Cys Gly Gly Arg Arg 35	
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gct coa ato gto agg gac gaa tgc tgt age gat cct agg tgt cac ggg Ala Pro Ile Val Arg Asp Glu Cys Cys Ser Asp Pro Arg Cys His Gly 20 25	96
aat aat ogg gac cac tgt got tgaagacget getgetecag gaccetetga Asn Asn Arg Asp His Cys Ala $$35\ $	147
accacgacgt	157

<221> CDS

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<211> 39
<212> PRT
<213> Conus regius
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Ala Pro Ile Val Arg Asp Glu Cys Cys Ser Asp Pro Arg Cys His Gly
Asn Asn Arg Asp His Cys Ala
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<211> 156
<212> DNA
<213> Conus regius
<220>
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<222> (1)..(117)
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Ser Asp Gly Arg Asn Thr Ala Ala Asp Glu Lys Ala Ser Asp Leu Ile
tct caa act gtc aag aga gat tgc tgt tcc cat cct ctc tgt aga tta
Ser Gln Thr Val Lys Arg Asp Cys Cys Ser His Pro Leu Cys Arg Leu
                                                                        147
ttt gtt cca gga ctt tgt att tgaagacget getgetecag gaccetetga
Phe Val Pro Gly Leu Cys Ile
          35
                                                                        156
accacgact
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Ser Asp Gly Arg Asn Thr Ala Ala Asp Glu Lys Ala Ser Asp Leu Ile
Ser Gln Thr Val Lys Arg Asp Cys Cys Ser His Pro Leu Cys Arg Leu
Phe Val Pro Gly Leu Cys Ile
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133	
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gct caa atc gtc agg aga gga tgc tgt tcc cat cct gtc tgt aaa gtg Ala Gln Ile Val Arg Arg Gly Cys Cys Ser His Pro Val Cys Lys Val 20 25 30	i
agg tat cca gac ctg tgt cgt tgaagacgct gctgctccag gaccctctga $$\rm 14$$ Arg Tyr Pro Asp Leu Cys Arg 35	7
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Ala Gln Ile Val Arg Arg Gly Cys Cys Ser His Pro Val Cys Lys Val $20 \hspace{1cm} 25 \hspace{1cm} 30 \hspace{1cm}$	
Arg Tyr Pro Asp Leu Cys Arg 35	
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aat aat coa cac att tgt ggt tgaagacget getgeteeag gaecetetga $$14$$ Asn Asn Pro His Ile Cys Gly $$35$$	17
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Ala Gln Ile Val Arg Arg Gly Cys Cys Ser His Pro Ala Cys Asn Val
Asn Asn Pro His Ile Cys Gly
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Ser Āsp Gly Arg Asn Āla Āla Āla Āsp Asn Lys Pro Ser Āsp Leu Ile
96
agg tat toa gac atg tgt ggt tgaagacgot gotgotocag gaccototga
Arg Tyr Ser Asp Met Cys Gly
                                                               157
accacgacgt
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Ala Gln Ile Val Arg Arg Gly Cys Cys Ser His Pro Val Cys Lys Val
Arg Tyr Ser Asp Met Cys Gly
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tot ggc ccc agg gga gga tgt tgt tcc cac cct gcc tgt aag gtg cat Ser Gly Pro Arg Gly Gly Cys Cys Ser His Pro Ala Cys Lys Val His 20 $_{\rm 20}$

ttt oca cac agt tg
t ggt tgacgacgot gatgotocag gaccototga Phe Pro His Ser Cys
 Gly

35

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15

144

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	ctt tgt cgt aga aga cgc tgatgeteca ggaccetetg aaccaegaeg t Leu Cys Arg Arg Arg Arg 35	145											
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His Pro Glu Ile Cys Arg
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acc gtc tgg gaa gga tgc tgt tct aat cct gcc tgt ctc gtg aat cat
Thr Val Trp Glu Gly Cys Cys Ser Asn Pro Ala Cys Leu Val Asn His
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gct cag atc gcc cat cga gac tgc tgt gac gat cct gcc tgc acc gtg Ala Gln Ile Ala His Arg Asp Cys Cys Asp Asp Pro Ala Cys Thr Val 20	96
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